RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

VOL. 35 AUGUST, 1940 NO. 2

# CLINICAL AND PNEUMO-ENCEPHALOGRAPHIC STUDIES IN PRE-SENILE DEMENTIA

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SINCE the original descriptions of A Pick (1892) and Alzheimer (1907), there have been a number of clinical and pathologic studies of the pre-senile dementias (1,2). Although the diagnostic value of pneumo-encephalography in these conditions is accepted without question, the published radiographs are few in number and their interpretations are somewhat confusing.

As these clinical syndromes are relatively unfamiliar to American radiologists, we will preface the presentation of a case history with a brief summary of the pertinent clinical and pathologic characteristics of these diseases. In this patient the diagnosis of a pre-senile dementia was made on clinical data and was supported by pneumo-encephalographic study. However, autopsy was not obtained and pathologic confirmation of the diagnosis was not possible.

*Pick's Disease.*—Pick's disease is a progressive dementia, occurring in women twice as often as in men, with its highest incidence in the sixth decade of life. Its cause is unknown. Heredodegenerative influences (Grünthal) and angiospasm (Ferraro and Jervis) have been suggested as causal factors. The onset is insidious, with gradual loss of interest in personal appearance and in daily affairs. The dementia is progressive, the mood becomes apathetic and speech appears stereotyped or repetitive. Memory is impaired although not as markedly as in Alzheimer's disease. Motor restlessness and motor perseverative actions are frequently observed but it is more common to observe akineses. Aphasic symptoms develop. Eventually the deterioration progresses to a vegetative dementia. Convulsive seizures may occur late in the course of the disease. Extra pyramidal rigidity of the limbs has been observed. The course of the illness is usually between three and five years, although there are extremes of from two to twelve years. Laboratory examinations, excluding pneumo-encephalograms, reveal no significant data.

Grossly, the brain shows evidence of diffuse atrophy with localized, symmetrical areas of marked shrinking. These localized atrophies involve the frontal lobes, the first and second temporal convolutions, the insulæ, the supramarginal and the angular gyri. Occasionally the parietal and occipital lobes are involved. The pre- and post-central gyri are free from any involvement. The weight of the brain is reduced (usually less than 1,000 grams) and the left hemisphere usually weighs less than the right. Microscopic examination of the involved areas shows loss of nerve cells in the cortex with glial replacement. The presence of

intracellular argentophil inclusion bodies remains of questionable significance. Signs of acute softening or of inflammation have not been observed. Arteriosclerotic vessels, senile placques, and Alzheimer intracellular fibrillary changes are found infrequently and are considered to possess no special significance.

Pick's disease must be differentiated from paresis, brain tumor, senile dementia, and cerebral arteriosclerosis. Most difficult of all is the differentiation from Alzheimer's disease.

*Alzheimer's Disease.*—Alzheimer's disease is also a progressive dementia. Its cause is, likewise, unknown. Most investigators have believed that it is a pre-senile disease and associated in some manner with the aging process. Its appearance in younger individuals after toxic or infectious episodes and its occasional familial incidence have raised the question as to the homogeneity of this syndrome. It occurs slightly more frequently in women than in men; the age incidence is roughly comparable to that of Pick's disease. The average course of the disease is from five to seven years, although there have been clinical reports of patients living 20 years after the onset of mental symptoms. The onset is gradual but the mental deterioration and loss of memory are more rapid than in senile dementia. Prolonged periods of motor restlessness, confusion, and anxiety are encountered in the course of the disease. Speech disturbances include paraphasia, perseveration, and logoklonia. Apraxia is common. Convulsive seizures and syncopal attacks have been observed. Cortical blindness, muscular hypertonicity, pupillary disturbances, facial paresis, sensory changes, and pyramidal tract signs may occur.

Macroscopic examination of the brain reveals a diffuse degeneration of the cerebral cortex, most marked in the frontal lobes. Microscopic examination of the cortex reveals degeneration of the ganglion cells of the cortex, the presence of large numbers of senile placques, which are silver-staining, star-shaped masses of undetermined origin, and the Alzheimer intracellular fibrillary distortion of the ganglion cells.

As stated previously, the differentiation between Pick's and Alzheimer's diseases is very difficult. Certainly, there is no pathognomonic sign or symptom in either. The distinction must be based on an evaluation of all the signs and symptoms and on the evolution of the disease. Kahn and Thompson (3) pointed out the resemblance of Pick's disease to paresis and of Alzheimer's disease to senile dementia. Memory loss occurs earlier and is more profound in Alzheimer's disease. Confabulatory tendencies are more common in Alzheimer's disease. Convulsive seizures may occur in both, but their occurrence early in the disease would favor a diagnosis of Alzheimer's disease. Hyperkinesis and episodes of motor restlessness may occur in both. Focal neurologic signs and symptoms occur more frequently in Alzheimer's disease.

*Case Report.*—H. G. B., 62-year-old housewife, was admitted to the Peter Bent Brigham Hospital on Nov. 30, 1939, with the presenting complaint of confusion, which had been progressive over a period of four years. The mother of the patient was said to have had a mental disease similar to that of the patient.

The patient's past medical history revealed no significant data. She was described as a well educated woman who had managed household affairs adequately previous to the onset of the present illness. She had few interests outside the home except for participation in the family's business enterprises. She had always been emotionally labile, experiencing sudden episodes of irritability and suspicion in her relations with her husband and children.

Approximately four years before admission the family noted that the patient was becoming careless of her personal appearance, that her memory was impaired, and that her somewhat mercurial mood had become much more tranquil. She had subjective sensations of numbness in the fingers of the left hand and complained of inability to see from the lower half of her

left eye. Hospital examination at that time revealed glycosuria. She was placed on a low carbohydrate diet. In the course of the next two years her confusion increased. She complained no longer of numbness of the left hand but vision of the left eye diminished and was finally lost. She lost initiative in her daily tasks and interest in her family, was apathetic and had to be forced to move about from place to place. She would forget that she had eaten and would return to the kitchen to gorge herself with food at frequent intervals. Her speech became limited in scope and occasionally she would reiterate phrases. She would sleep for periods of from 14 to 16 hours at one time, arise to gorge herself with food only to return to her or another's bed.

Three months before admission the patient was sent to a convalescent home where she remained for one week but decided to return home as she believed the care was inadequate. This was cited by the informants as the most decisive action the patient had made in the past four years. No evidences of illusions, hallucinations, or delusions were observed by the informants.

Five days before admission the patient was found on the floor in an unarousable stupor. She regained consciousness the following day with no essential change in her mental status. However, since then the patient had been incontinent of feces and urine. It had also become more difficult to communicate with her.

Physical examination on admission revealed no essential findings. Heart and lungs were normal, blood pressure was 170/90, laboratory examinations, including spinal fluid, were within normal limits.

Neurologic examination showed the following findings: The pupils were equal; they reacted to light briskly. The convergence reflex was absent and there was weakness of the right internal rectus muscle. She appreciated light, but not fingers, with the left eye. The disc margins were distinct; there was a slight degree of narrowing of the retinal arteries. There was a right lower facial paresis. The arms and legs showed cogwheel rigidity with passive movement; slight tremor of outstretched fingers, left greater than right; increased deep reflexes, bilateral finger jerks and Hoffmann signs; bilateral grasp reflexes, and the tonic foot reflex was greater on the right than on the left. Finger-to-nose test was done well but patient was unable to do heel-to-knee test. As far as could be determined sensation was appreciated normally. She recognized objects placed in her hands. She was incontinent of urine and feces.

Psychiatric examination showed the patient to be apathetic and vacuous. She was disoriented for time and place. Her defects in memory were considerable and involved recent and remote events. She retained three digits forward, none backward, and was unable to recall after two minutes. She did not confabulate. No delusional content or sense deceptions were noted. Her speech was never spontaneous and her answers were economical, *i.e.*, she usually repeated the question which had been given to her. At times she was able to carry out some commands; at other times she did not appear to understand anything. She was not aphasic but was markedly perseverative. This perseveration was observed in her speech, in recognition of objects by sight or by touch, by copying simple geometric designs, and in repetitive motor movements. She was apractic, being unable to write or to use a fork. She was not able to interpret fables or proverbs or to perform block tests.

After plain films of the skull had been obtained, pneumo-encephalography was done on Dec. 7, 1939, at which time 180 c.c. of cerebrospinal fluid were removed and 170 c.c. of air injected. The patient experienced no untoward reactions during the procedure, although her blood pressure became elevated at the conclusion of the operation and she experienced a transient stupor with weakness of the right side. Her course remained essentially unchanged for the next few days although she did not respond as well as she had. Bilateral suck-

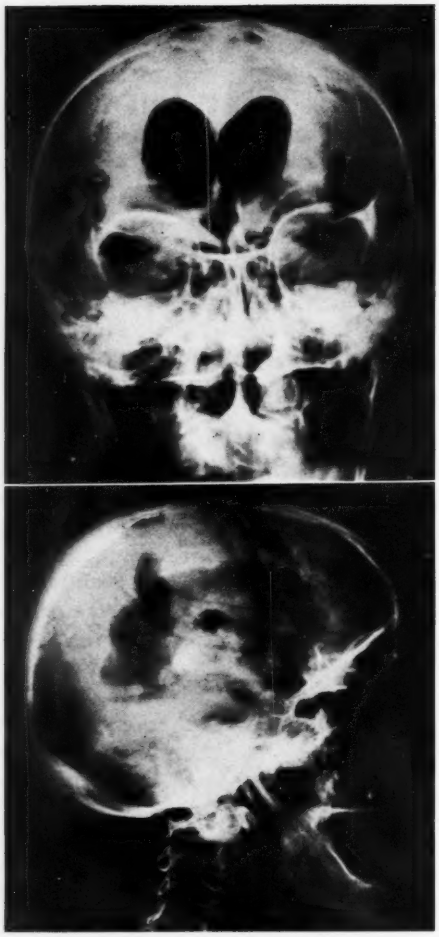

Fig. 1 (*above*). Anteroposterior view in supine position showing rather marked symmetrical dilatation of both lateral ventricles including the temporal horns and of the third ventricle. The triangular collections of air around each island of Reil are well shown just above and lateral to the tip of each temporal horn.

Fig. 2 (*below*). Left lateral view in prone position showing marked dilatation and "ribbing" of the right lateral ventricle. Dilatation of temporal horn is less marked. The deep, irregular sulcus (? along sylvian fissure) is well shown.

ing reflexes were obtained and the weakness of the total right side appeared more marked. Terminally, following the parenteral introduction of glucose she showed sugar in the urine and a markedly elevated blood sugar. She developed a stiff neck and lumbar puncture revealed grossly bloody spinal fluid which was withdrawn with a syringe as pressure determinations could not be done. The possibility of a cerebral hemorrhage was considered at this time. She died on Dec. 17, 1939.

*Discussion of Case.*—Progressive dementia occurring in a patient of this age necessitated consideration of a number of organic brain diseases. General paralysis was excluded by the absence of history of infection, the duration of the illness without treatment, and the negative blood and spinal fluid serology. Neoplasm was excluded by reasons of duration of illness, absence of increased pressure, diffuse neurologic findings, and the profound dementia. Senile dementia usually occurs at an older age period and the mental deterioration is characterized by memory defect with falsification and confabulation. Rarely is there such a profound dementia in a short period of time nor are there focal neurologic signs. Presbyophrenia usually resembles senile dementia in its symptomatology. Cerebral arteriosclerosis usually has more physical signs of arterial disease, focal neurologic signs are sudden in onset and regressive in character. The dementia is rarely as progressive and mood is apt to be unstable and irritable rather than apathetic.

This differentiation led to a consideration of the rarer pre-senile dementias, *i.e.*, Pick's and Alzheimer's diseases. Because of their rarity, any such diagnostic impression is hazardous. Although the patient did have evidences of cerebral arteriosclerosis, diabetes, and possibly of cerebral hemorrhage, the total clinical picture did not fit into the usual understanding of these diseases. It was impossible, from a clinical point of view, to arrive at a specific diagnosis of either Pick's or Alzheimer's disease. Pneumo-encephalographic studies added interesting data which seemed to support the clinical diagnosis of a presenile dementia and favored the diagnosis of Pick's disease.

The plain films of the skull were negative except for bilateral calcification of the internal carotid arteries seen on either side of the sella turcica. On the eighth hospital

day pneumo-encephalograms were made which showed a symmetrical dilatation of the lateral ventricles without displacement. The anterior horns, lateral ventricles, and posterior horns measured 3, 4, and 4 cm., respectively, in transverse diameters. The third ventricle was also dilated though not displaced and measured 1.7 cm. in transverse diameter. Associated with these findings there were abnormal triangular collections of air just lateral to each island of Reil measuring about 3 cm. in diameter (Fig. 1). In the lateral views no air was seen over the cortex except one large deep sulcus 1.5 cm. in diameter which ran obliquely over the right parietal area. This was thought to be along the sylvian fissure. The basal cisterns were not well filled (Fig. 2). These findings were interpreted as indicative of internal hydrocephalus with cortical atrophy. This was most marked in the temporal regions. Pneumo-encephalograms in Pick's disease have shown similar localized atrophies. The other point of particular interest in this case was the peculiar scalloped appearance of the bodies of the lateral ventricles. This condition is known as "ribbing of the ventricles" (Dyke and Davidoff, 4) and is seen occasionally in cases with marked ventricular dilatation regardless of the cause. It is believed that the scalloped effect is due to the disparity between the elasticity of the blood vessels and the white matter, the former being more fixed while the white matter recedes. The condition has no pathologic significance in itself.

*Pneumo-encephalographic Studies in the Pre-senile Dementias.*—Pneumo-encephalography is considered to be of definite value in the diagnosis of the pre-senile dementias and in the differentiation between them. Bumke (5) described a patient with Pick's disease in whom pneumo-encephalography had been performed. The radiograph which was included in a later description (1936) was interpreted as showing an increase of subarachnoid air in the frontal region and a dilatation of the anterior portion of the lateral ventricles. Unfortunately, the quantity of air introduced and the method employed is not known and the single film is far from being conclusive of frontal lobe atrophy. Pneumo-encephalograms of a patient with Alzheimer's disease are included in this later report (Bumke and Foerster, 5). Other than symmetrical dilatation of the lateral ventricles without displacement and indefinite collections of air laterally, it is difficult to see other abnormalities.

Flügel (6) published a case history of a patient with Alzheimer's disease with pneumo-encephalographic study, showing slight dilatation of the ventricular system and a considerable amount of air in the subarachnoid spaces of the convexity. General cerebral atrophy was assumed from these encephalograms. Unfortunately, no radiographs are included in his report. In 1932, Flügel (7) wrote a very detailed review of encephalography and discussed the differential diagnosis of Alzheimer's and Pick's diseases. He stressed the fact that broad stripes of air over the convexity are seen in Alzheimer's disease, while in Pick's disease there are large confluent masses of air in the temporal and frontal regions. There are no radiographs of Pick's or Alzheimer's disease included in this report.

Kahn and Thompson (3) were in agreement with Flügel's observations but included no radiographic data.

Lemke (8) studied a patient with Pick's disease and included an encephalogram. This showed an accumulation of air in the frontal region and an accentuation of the subarachnoid cortical markings.

Freeman (9) illustrated a review of the pre-senile dementias with a brief clinical case report and encephalogram of a patient studied by Shapiro. Neither the case history nor the encephalogram was conclusive of Pick's disease. The latter appeared to demonstrate the presence of subdural air over the convexity rather than any localized lobar atrophy.

Nichols and Weigner (1) included antero-posterior and lateral encephalograms of a patient with Pick's disease. These were interpreted to have symmetrical dilatation

of both lateral ventricles, more marked in the anterior horns. The cortical markings were not normally distributed and were stated to be dilated four or five times their normal width, indicative of considerable cortical atrophy. In the radiographic reproduction this dilatation of cortical markings is not conspicuous. However, there seems to be an accumulation of air outlining the insulæ.

Erdelyi (10) published encephalographic observations of a patient with Pick's disease which had been previously reported by Benedek and Horanyi. After cisternal puncture, 30 c.c. of fluid were removed and 25 c.c. of air introduced. Erdelyi stated that large amounts of subarachnoid air were noticed in the frontal region and that the accumulation of air produced large spots or band-like shadows. He added that partial subarachnoid filling was visible bilaterally in the temporal areas. He interpreted these findings as extensive atrophy of the frontal lobes and slight atrophy of the temporal lobes. The atrophy was more pronounced in the left side. The bands or stripes of air are not perceptible in the reproductions.

Benedek and Lehoczky (11) reported three patients with Pick's disease. Their report considered the clinical recognition of the disease utilizing pneumo-encephalography, arteriography, and brain puncture. One of their patients had been reported by Erdelyi (10). The remaining two patients revealed interesting encephalographic data. In one there were distended lateral ventricles with a dilated cavum septi pellucidi (fifth ventricle). There was an increase in the intergyral spaces presenting a stripe-like aspect with confluent masses, especially over the frontal region. Only an anteroposterior view of the encephalogram of the third patient is presented. This shows tremendous symmetrical dilatation of the anterior horns with a marked accumulation of air in the temporal regions. The authors called these collections of air "opercular cysts." They stated that repeated encephalograms demonstrated an increase in the temporal lobe air and suggested that this was evidence for progressive atrophy of the operculum. Anteroposterior and lateral ventriculograms are also included of this patient. They showed a dumb-bell configuration of the lateral ventricles with enlargement of the anterior and temporal horns.

Fromenty (12) reported the encephalographic study of four patients. It is stated that there is autopsy verification of Pick's disease in the first patient. The second and third patients were suspected to have Pick's disease, the fourth patient was epileptic. In the proven case of Pick's disease, as well as the two suspected cases, there was bilateral asymmetrical dilatation of the lateral ventricles and accumulation of air in the frontal and temporal regions. However, in the reproduced radiograph which illustrated the case report of the third patient, the author interpreted the film as showing asymmetrical ventricles, left larger than right, tremendous atrophy of the right pre-frontal pole which extended over to the left and along the falx cerebri. It is quite possible that the accumulation of air over the convexity is subdural air which has compressed the ventricle of the same side.

Brain (13) included an encephalogram in his review of the pre-senile dementias. He noted the excess of air over the frontal cortex and the enlarged ventricles. While there is an increase in the intergyral cortical markings of the frontal lobes, there does not seem to be any marked dilatation of the ventricles. Unfortunately, he did not give the clinical description or the specific diagnosis.

The patient with Pick's disease reported by Malamud and Boyd (14) had autopsy evidence of circumscribed symmetric atrophy of the temporal lobes. Yet, encephalography performed four years before death showed only moderate and symmetric dilatation of the lateral ventricles.

With the exception of the radiographs reproduced in Bumke and Foerster (5) we were unable to find any encephalograms of patients with Alzheimer's disease. These films showed the dilated ventricles and indefinite air collections laterally but did

not resemble the broad stripes of air over the convexity which were thought by Flügel to be characteristic of the diffuse atrophy (1932).

On the other hand, there seems to be considerable agreement in the pneumo-encephalographic data in Pick's disease. These included bilateral dilatation of the lateral ventricles, increase of intergyral air spaces more marked in the frontal and temporal areas, and accumulations of air over the frontal and temporal lobes in the nature of confluent masses.

## SUMMARY AND CONCLUSIONS

1. Pick's disease and Alzheimer's disease are progressive pre-senile dementias, characterized by more or less specific gross and microscopic brain atrophy.

2. The case history of a patient with pre-senile dementia is presented. Clinical study and encephalograms supported the diagnosis of a pre-senile cerebral atrophy. Lack of necropsy confirmation prevented further differentiation between Pick's and Alzheimer's diseases.

3. In addition to demonstrating bilateral dilatation of the lateral ventricles and confluent masses of air over the temporal regions, the encephalogram in this patient showed ribbing of the ventricles indicative of internal hydrocephalus.

4. The available literature concerning encephalographic studies in these diseases has been reviewed. We were not able to find any published radiographs of Alzheimer's disease to conform with Flügel's description. On the other hand, there is considerable agreement in the encephalographic studies in Pick's disease.

5. It is hoped that the presentation of this report will lead to an increased awareness of the pre-senile cerebral atrophies and to further study of the pneumo-encephalograms obtained in these patients.

We wish to express our appreciation of the aid given to us in this study by Merrill C. Sosman, M.D.

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# THE RADIOLOGICAL SOCIETY OF NORTH AMERICA STANDARDIZATION COMMITTEE, TECHNICAL BULLETIN NO. 1*[1]

*By* EDITH H. QUIMBY *and* GEORGE C. LAURENCE, Members of Subcommittee

## THE MEASUREMENT OF DOSE IN ROENTGEN THERAPY

### CHAPTER I.—THE MEANING OF DOSE, EXPOSURE, AND OTHER PHYSICAL TERMS USED

AS the art of radiology has developed, the significance of many of its technical terms has been altered, modified, or broadened to suit new methods or to conform with new knowledge. The meanings of the physical terms have now become fairly well established; nevertheless, the earlier changes have resulted in a vagueness in the use of these words that is responsible for many of the difficulties encountered in measuring x-rays. The terms that are used in this bulletin are discussed below with attention to some of the misunderstandings that frequently lead to difficulties.

The *exposure* or *dose*[2] is a measure of a property of the x-rays at a particular place. This place may be situated in air, in tissue or other material, or even in vacuum. The exposure is expressed as a number of roentgens.

The exposure is a property of the radiation only. The number of roentgens is a partial description of the x-rays at the place where it is measured or calculated. It tells nothing about what happens to the radiation or about the effects which it produces. It does not indicate whether the radiation is absorbed or passes through the region without absorption. It tells nothing about the material which it penetrates. It applies only to the radiation itself.

The average *exposure rate*, *dosage rate*, or *intensity* is obtained by dividing the exposure by the time required to deliver it. Hence the exposure is the product of the average exposure rate and the length of time it continues. The exposure rate is usually expressed in roentgens per minute.

The exposure may be measured with an instrument called *a dosemeter*, *exposure meter*, or *roentgen meter*. The dosemeter is intended to measure the exposure only. The reading obtained with the instrument should not be considered as a measure of the absorption of the radiation or of the ionization produced by the radiation. The absorption and ionization necessary to operate the instrument are not the effects that the dosemeter has been calibrated to measure. Exposure, absorption, and ionization are three very different physical effects and should be distinguished clearly.

Furthermore, the difference in exposure at two places, one of which is farther from the x-ray tube, is not a measure of the energy absorbed between the two places. The difference is due to three causes: divergence of the radiation, true absorption, and the presence of scattered radiation.

The *divergence* of the radiation refers to the increase in cross-section of the x-ray beam as the distance from its source increases. This increase in size of the x-ray beam implies that the radiation is more widely distributed and, therefore, less intense. The intensities (exposure rates) at points along the central axis of the x-ray beam are inversely proportional to the squares of the distances from the focal spot of the x-ray tube *if there is negligible absorption between the points and negligible scattering from objects in the beam.*

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* The Editor wishes to state that extra copies of this Bulletin may be obtained from the Secretary, D. S. Childs, M.D., 607 Medical Arts Bldg., Syracuse, N. Y., at a small cost.

[1] Approved at the Twenty-fifth Annual Meeting, at Atlanta, Dec. 11–15, 1939.

[2] The two terms "exposure" and "dose" are used interchangeably in this text. "Exposure" is preferred because it calls attention to the fact that it describes the radiation to which the place is exposed. "Dose," by unfortunate association of ideas, may suggest incorrectly that it refers to the radiant energy that is absorbed. (See third paragraph of the text.) The older term, "quantity," which is unsatisfactory, is avoided.

Example: At 25 cm. from the focal spot the exposure is 150 r. Hence at 50 cm. from the focal spot the exposure is

$$150 \text{ r} \times \frac{25 \text{ cm.} \times 25 \text{ cm.}}{50 \text{ cm.} \times 50 \text{ cm.}} =$$

$$150 \text{ r} \times 1/2 \times 1/2 = 37.5 \text{ r.}$$

This rule is called the *inverse square law*. It applies only to radiation received directly, without scattering or absorption, from a small source such as the focal spot of the x-ray tube. Hence it should not be used for accurate calculation of the exposure in cases in which there is appreciable scattered radiation, *e.g.*, near the filters, cooling oil, and the aperture of the treatment cone if the inner surface of its walls is exposed, near walls and furniture, or when the patient is in the x-ray beam. Since scattered radiation is difficult to avoid, the inverse square law is more useful for approximate estimates in planning treatment than for the final determination of the exposure. The inverse square law enables us to calculate the effects of divergence, but it does not take into account the two other factors that can contribute to the difference in exposure at two places: absorption and the presence of scattered radiation.

The word *absorption* is used in radiology with a restricted technical meaning which should not be confused with its more general significance or with casual colloquial usage. Technically, absorption involves two processes, *viz.* (1), deflection or change in direction of some of the photons[3] of the x-ray beam, and (2) change of quality or complete disappearance of some of the photons by transfer of their energy to the material to produce fast corpuscular rays. As the radiation travels through the material, the number of photons that have not been deflected or otherwise altered continues to decrease. This decrease is due to absorption.

The energy lost from the original beam is not entirely consumed at the place where the absorption occurs, but is transmitted elsewhere by the deflected x-rays and by the fast corpuscular rays that are produced. *Hence absorption does not refer to the amount of radiant energy that is made available for producing biological effects* at the place where the absorption occurs.

*Scattering* refers to the change in direction of propagation of the radiation, caused by the deflection of the rays from their original direction as mentioned above. *Scattered radiation* refers to the rays received at the place of measurement, that have been so deflected in other parts of the material and in other objects exposed to the radiation.

*Primary radiation* is the radiation that is received directly from the focal spot of the x-ray tube. The inverse square law applies accurately to the primary radiation, except within a short distance of the target, or when there is no absorption along the path of the radiation.

*Secondary characteristic x-radiation* is x-radiation which *originates* in any material that is exposed to x-rays. It is difficult to distinguish in measurement from scattered radiation and is usually of relatively low intensity. In common practice the distinction is ignored, and the term "secondary radiation"[4] is used to include both scattered and secondary characteristic radiation.

*Total radiation* includes all x-rays arriving at the place where it is measured. The *total exposure* is the sum of the primary radiation and the secondary (scattered plus secondary characteristic) radiation exposures.

*The free air exposure* is the exposure of radiation received from the x-ray apparatus in a region in air where the exposure of scattered radiation from objects external to the x-ray apparatus (*e.g.*, the patient and the walls of the room) is negligible. It is due to primary radiation and radiation

[3] The energy of a beam of x-rays may be considered to be divided into a very large number of parts called photons. Usually one photon only is involved in the interaction of the radiation with one atom of the material.

[4] Reference to the secondary radiation as "scattered radiation" is a common misuse of terms. For example, "back-scatter" consists of both scattered and secondary characteristic radiation.

scattered from internal parts of the x-ray apparatus and treatment cone, *e.g.*, filters, cooling oil, etc.

The *tissue exposure* is the total exposure at a place in tissue. It is useful sometimes to consider the tissue exposure as consisting of two parts: primary and secondary. *Primary tissue exposure* is the part of the tissue exposure due to primary radiation and radiation scattered from internal parts of the x-ray apparatus. *Secondary tissue exposure* is the remaining part of the tissue exposure, and is due to scattered and secondary characteristic radiation from the tissue and other objects external to the x-ray apparatus. It should be noticed that the words "primary" and "secondary" are not entirely appropriate in these terms and may be misleading.

The *skin exposure* is the tissue exposure at a place very close to the skin surface. It is possible to determine the skin exposure approximately by measuring the exposure in air very close to the skin surface, because the exposure does not alter abruptly in passing through the surface from air to tissue but changes gradually. Thus the exposure at a point 0.1 mm. above the surface does not differ very greatly from the exposure at a point 0.1 mm. below the surface, even though the two points are in different materials. (This follows from the fact, stated earlier, that the exposure describes the radiation but not what happens to it.)

In describing a treatment, either the free air exposure or the tissue exposure may be specified (often both are desirable). The former applies to the radiation that would have been present at the point considered if the patient and other scattering and absorbing objects were removed from the x-ray beam; the latter applies under the actual conditions of the treatment with the point occupied by tissue. The two values of the exposure usually differ greatly, and it is essential to indicate clearly which is intended. Such statements as "the patient received 1,000 r" are meaningless. Ambiguity should be avoided by the use of such expressions as: "free air exposure of 1,000 r at the skin surface," "skin exposure of 1,000 r," "free air exposure of 1,000 r at 5 cm. below the skin surface," "tissue exposure of 1,000 r at 5 cm. below the skin surface," or by other precise description. *The word "exposure" should never be used without preceding it by the words "free air," "skin," or "tissue"* unless it is clear from context or explanation which is meant. *The exposure should never be specified without indicating where the exposure applies* (*e.g.*, distance below skin surface, distance from cone, or otherwise). *A treatment should never be described by stating the number of roentgens without further explanation.*

X-rays are a form of energy propagated through space. It would be useful to measure the quantity of radiant energy passing through unit area at any particular place during a treatment, but this is not easily done. Measurement of the exposure in roentgens has, therefore, been adopted as a practical substitute for the measurement of the flow of energy, and our methods of dosage specification have been based entirely on measurement of exposure instead of energy. The energy of the radiation, flowing through a region or absorbed in it, is not measured and for practical purposes need not be considered. In fact, energy is mentioned here only to emphasize that *the exposure is not a measure of the energy of the radiation.* Exposure is related to a different property of the radiation, *viz.*, its ability to ionize air under certain specified conditions. It is not possible to deduce the flow of energy or the absorption of energy from knowledge of the exposure only. The flow of energy in an exposure of one roentgen of very hard x-rays is much greater than in the same exposure of very soft x-rays. The absorption of energy with an exposure of one roentgen is much greater in a dense material like tissue than in a material like air. Moreover it is not possible to deduce the attenuation of the intensity of the radiation in penetrating a material from the exposure alone. Hard radiation is more penetrating in tissue than soft radiation regardless of the skin exposure.

When rays penetrate matter, *secondary*

*corpuscular rays*[5] are produced, which are electrons expelled from atoms of the matter with very high velocities by energy received from the x-rays. These secondary corpuscular rays produce nearly all of the ionization that occurs when x-rays pass through matter. The number and energy of the secondary corpuscular rays that are produced depend on the material traversed, as well as on the quality of the primary beam. This fact has two consequences of particular importance in practical radiologic measurement.

First, the walls of the thimble ionization chamber that is used to measure the exposure of x-rays must be thick enough to prevent any secondary corpuscular rays that are produced in material outside the chamber from passing through the walls; otherwise, the number of ions produced in the chamber would be affected by these secondary corpuscular rays from the outside material and the instrument would not record the exposure correctly. (The use of very thin wall chambers should not be attempted without clear understanding of the physical principles involved and of the properties of the rays.)

Second, to permit a consistent relation between the skin exposure and the reaction it produces, *the material directly over the skin must be suitably chosen*, particularly when using very hard x-rays. The skin tissue receives secondary corpuscular rays from the material next to it and hence the reaction depends partly on the nature of the material. To obtain consistent results, the material should not differ greatly in x-ray absorption properties from the tissue. Commercial bakelite and other impregnated composition materials are suitable and convenient for this purpose. If the aperture of the treatment cone is not provided with a window or cover of this material, a sheet of it should be placed over the skin. (Most treatment cones recently manufactured are so provided.) It is particularly important to protect the skin from secondary corpuscular rays from lead glass or any metal that is exposed to the x-rays. The thickness of bakelite, either in the cone window or otherwise covering the skin, required for this protection, is at least 0.3 mm. for every 100 kv. peak potential applied to the x-ray tube. However, an air space of at least 5 cm. between the skin and the lead parts of the diaphragm system, as occurs in the use of open ports without cones, provides the necessary protection if the tube potential is less than 250 kv. and the width of the treatment field at least 5 cm. (See also Chapter V.)

[5] The secondary corpuscular rays are sometimes called "secondary beta rays." The latter term is inappropriate because beta rays are of radio-active origin. (The term "corpuscular rays" is applicable to any small particles projected with high velocity, *e.g.*, alpha particles, neutrons, etc., but in x-ray therapy we are concerned only with electrons.)

## CHAPTER II.—INSTRUMENTS AND APPARATUS

*Portable Roentgen Meters (Dosemeters) with Thimble Ionization Chambers.*—Portable dosemeters or roentgen meters with small ionization chambers, known as "thimble chambers," are calibrated to read the exposure in free air that would occur at the point occupied by the center of the chamber if the instrument were removed. They record the total exposure of radiation received from all directions. They are calibrated with the axis of the chamber placed perpendicular to the axis of the x-ray beam, and they may be less accurate if used with the chamber axis in other directions. Hence the axis of the chamber should be placed at right-angles to the direction from which the greatest intensity of x-rays is received. Small thimble chambers are preferable to larger ones for measurements in a phantom because the displacement of the phantom material by their presence is a source of error.

Portable roentgen meters should be recalibrated at regular intervals unless they are checked by exposure to the radiation from a radium needle or checked by comparison with other roentgen meters. The use of a radium source consisting of a few milligrams of radium element is the only

method of checking the calibration of such a roentgen meter without recourse to comparison with another roentgen meter or a standard ionization chamber.

It is recommended that a radium check machinist, to fit the chamber support snugly, and marks should be engraved on the needle and chamber to assist in accurate replacement.

Many roentgen meters are provided with

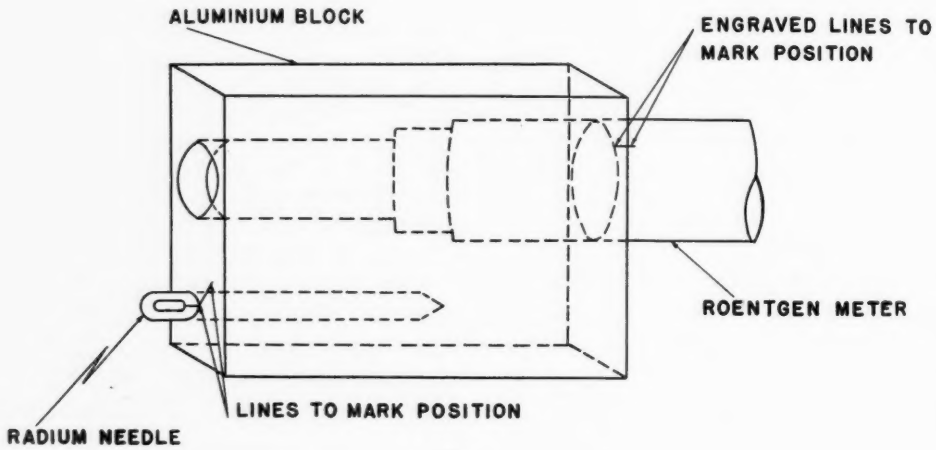


Fig. 1.

be provided for the thimble chamber roentgen meter. This may consist of a small radium needle or tube (5–10 mg.) and a metal holder to mount the radium container at a fixed distance (about 1 or 2 cm.) from the thimble chamber (see Fig. 1). When the instrument is received from the manufacturer, or has just been calibrated, the intensity of the radiation from the needle should be measured by the instrument in terms of the number of divisions of the scale traversed per minute. The instrument may be checked on later occasions by repeating this measurement. In making tests of this kind, it is necessary that the needle be replaced in the same position as accurately as possible, *e.g.*, the distance of the needle from the chamber should not vary by more than the thickness of a sheet of writing paper; the position of its ends should be set with similar accuracy; the needle should "point" in the same direction relative to the chamber, and the same sides of the needle and the chamber should be opposite each other. Hence, the metal holder should be made by a skilled

a device for testing the recording part of the instrument, *e.g.*, a switch (usually marked "test") for discharging a part of the electrical circuit, or an auxiliary ionization chamber containing a small quantity of radio-active material. These devices make it possible to verify that the electrometer or the recording part of the instrument is operating properly, but they are not a means of testing the ionization chamber. Hence, they do not provide an infallible test that the instrument continues to read correctly since last calibrated.

*Use of Thimble Chambers with Extra Hard X-rays.*—Satisfactory standard ionization chambers for the calibration of roentgen meters for use with extra hard x-rays were not developed until very recently, and the manufacturers have not been able to calibrate such instruments with radiation excited at potentials above 200 kv. A roentgen meter cannot be expected to read correctly with radiation that is not within the range of qualities for which it has been calibrated. (A few instruments that have been calibrated by the

manufacturers with potentials up to 200 kv. applied to the x-ray tube, have been found later to read correctly with potentials up to 400 kv., but it must not be inferred that this would be true of *any* instrument, even if made by the same manufacturer.)

A roentgen meter calibrated with 200 kv. radiation may be used for relative measurements in comparing treatments with higher kilovoltages, using the same installation under conditions that do not differ greatly, if the following precautions are observed:

1. The instrument reading is interpreted in relative arbitrary units—not in roentgens.

2. The radiation used in the different treatments being compared does not differ greatly in quality, *e.g.*, the kilovoltage is not altered by more than 20 per cent.

3. The thickness of the wall of the ionization chamber is increased by covering with a sleeve of organic material of suitable thickness. A sleeve of unit density organic material should have a thickness of 0.3 mm. for every 100 kv. in excess of 350 kv. This precaution is unnecessary if the thimble chamber is surrounded on all sides by biological tissue, phantom material, bakelite, or similar organic products, for a distance equal to at least 0.4 mm. for every 100 kv. in excess of 350 kv.

4. The electrometer part of the roentgen meter is kept out of the x-ray beam and any appreciable scattered radiation.

5. Air spaces in the instrument, likely to give rise to spurious ionization currents, are kept out of the beam or adequately shielded.

*Ionization Chambers Mounted in the X-ray Tube Housing or in the Detachable Treatment Cone (Iometers, etc.).*—These instruments register the intensity of the radiation emitted by the x-ray tube in arbitrary units, at an undefined position in the tube housing. They enable the radiologist to ascertain that the radiation output of the apparatus is the same during treatment as during the preliminary or subsequent intensity measurements. They are also a valuable safeguard against unforeseen changes in the performance of the x-ray apparatus that might otherwise not be observed.

The proper use of these instruments is described in Chapter VI.

*Recording or Integrating Roentgen Meters.*—These instruments record the total exposure (or the total dose) delivered during a treatment. The recording part of the instrument is mounted on the technician's desk, the wall, or the control panel, and is connected through a flexible cable to the proper electrode of a vacuum tube, to which is also connected a thimble ionization chamber, which remains in contact with the patient's skin during the treatment. The chamber is either attached to the window of the treatment cone, or is supported on an adjustable bracket. The former type is neater and not likely to be moved from the field accidentally. The latter type is generally more useful because it can be moved about to explore the radiation field if desired, or used in a phantom, and it is more readily calibrated. Both types may be used for the measurement of free air exposure or skin exposure by the methods described in later chapters for portable roentgen meters.

It is recommended that recording roentgen meters be calibrated more frequently than the simpler types of instrument meter, because their complicated mechanism is more likely to get out of order.

The skin directly under the supporting stem of an ionization chamber that is left in place during the treatment receives a slightly smaller exposure than the rest of the field. This partial shadow on a small part of the field is obscured by scattered radiation and is unimportant below a depth of a few centimeters.

*Thin Wall Ionization Chambers.*—Ionization chambers having walls so thin that they are easily penetrated by nearly all of the secondary corpuscular rays reaching them from material outside the chamber are useful for investigating these secondary corpuscular rays. Measurements made with these thin wall chambers are suitably

expressed in "electrostatic units per cubic centimeter," abbreviated "e.s.u./c.c."

Under certain conditions only, the exposure of x-rays may be deduced from measurements made with thin wall chambers. Under these conditions very accurate measurements, suitable for the compilation of tables of data, may be made. Such use should be made only with a knowledge of the properties of the secondary corpuscular rays, and is not recommended for routine clinical work.

*Standard Ionization Chambers.*—Standard ionization chambers are unsuitable for the measurement of dose in the ordinary hospital or clinic. The accuracy implied by the term "standard" is attained only when they are used in the measurement of almost parallel primary radiation emitted from a small source. This requirement can seldom be met with hospital equipment. The principal function of a standard ionization chamber is the calibration of thimble chambers.

*Meters on the Control Panel of the X-ray Apparatus.*—Technicians should be trained to watch the various instruments and meters on the control panel. They should be particularly alert to discover and correct any unusual change in the kilovoltage or milliamperage during treatment, and to reproduce the readings of these instruments that were recorded when the dosage measurements were made, or the radiation output of the apparatus was measured. This precaution is particularly important if the installation is not equipped with a monitoring device, such as an ionization chamber in the tube housing. Careful attention to the meters should not be relaxed because the apparatus has operated satisfactorily in the past—defects and failures in x-ray apparatus usually occur unexpectedly.

*Treatment Cones or Applicators.*—Consistent relation between the skin dose and the skin reaction cannot be expected unless the material directly over the skin and in contact with it is always the same. This purpose is fulfilled by the cover made of bakelite or similar composition material that closes the end of the treatment cone placed against the skin. If the cover is removed, a greater or lesser reaction may result, depending upon the nature of the materials inside the cone that are exposed to the x-rays, owing to the secondary corpuscular rays that the skin receives. Tables of data such as are published in this bulletin apply more accurately if the cones are provided with baffles to define the width of the x-ray beam before it reaches the cover.

*Open Ports without Cones or Applicators.*—To insure consistent relation between dose and reaction referred to in the preceding paragraph, when open ports are used instead of cones, the patient's skin should be separated from the edge of the port, and other parts of the x-ray apparatus exposed to the x-rays, by a distance greater than the range of most of the secondary corpuscular rays. This distance should exceed 5 cm. for the radiation produced by 200 kv. or less. This limit should be increased by 5 cm. for each additional 100 kv. applied to the x-ray tube.

Care is necessary in using open ports to insure that the exposed part of the patient's body is moved as little as possible during the treatment. A change of a few centimeters in the distance of the tissue from the target of the x-ray tube results in considerable change in the exposure received. A lateral shift of less than a centimeter may, if the field is small, result in only a portion of the correct region being irradiated.

## CHAPTER III.—ACCURACY AND ERROR IN MEASUREMENT OF EXPOSURE

The busy radiologist has neither the time nor the facilities to measure exposure and dosage rate as accurately as the physicist in a standardization laboratory. He requires an accuracy that will assure him of reliable and consistent treatment. He will attempt to make these measurements as accurately as his equipment will permit without unduly increasing the labor and time required.

It is often difficult in the clinic to make measurements that can be relied on to be in error by less than 5 per cent. On the other hand, an error greater than 15 per cent can usually be avoided in the measurement of x-ray dosage for most treatments if moderate care is taken, and the directions given in this bulletin are followed.

Many causes may contribute to the error, *e.g.*, unsteady output of the x-ray tube, unavoidable differences between the conditions under which the measurement is made and the conditions under which the result of the measurement is to be used, inaccurate timing, carelessness in arranging the equipment, etc. If the total error is to be less than 15 per cent, the possible error due to each one of these causes should be considerably less than 15 per cent.

The fact must be accepted that accurate measurements require care. The attention to details stressed in the following pages may at first appear to be discouraging. To follow the recommendations faithfully will undoubtedly require more time and attention on the first occasion than the radiologist would be willing to devote to measurements in usual practice. However, it will be found that these methods will become familiar very quickly and will require very little more trouble than less careful measurements. The additional effort will be more than justified by the increase in confidence in the results obtained.

Invariably, measurements should be repeated, because inaccuracy is often revealed by disagreement in the measurements. However, close agreement of a number of measurements does not prove that they are accurate. *A large error may exist due to a cause that would not show itself by disagreement between readings*, e.g., *faulty arrangement of the apparatus, or an inaccuracy in the roentgen meter itself.*

The following directions are intended to supplement the instructions supplied by manufacturers of roentgen meters. Directions for making corrections for temperature, pressure, and altitude are not included since they are usually given in the manufacturers' instructions.

## CHAPTER IV.—MEASUREMENT OF THE FREE AIR EXPOSURE

1. *The roentgen meter should be suitable for the quality of the x-rays measured.* Most roentgen meters are fairly accurate for the measurement of radiation having a copper half value layer between 0.2 mm. and 4 mm. The quality at which the true calibration deviates seriously from the scale reading varies with different meters. The radiologist should verify that the instrument is suitably calibrated before using it under the following conditions:

(*a*) Voltages above 200 kv. (constant potential),
(*b*) Half value layer less than 0.2 mm. copper or 1.5 mm. aluminum,
(*c*) Voltages below 100 kv. (peak or constant potential) with a thick wall x-ray tube and no metal filtration,
(*d*) Voltages below 120 kv. (peak or constant potential) with a thin wall x-ray tube and no metal filtration,
(*e*) Voltages below 100 kv. (peak or constant potential) with a thin wall tube and 2 mm. aluminum filtration.

2. *Scattered radiation should be avoided.* This requirement will be adequately fulfilled if there are no objects except the roentgen meter chamber in the x-ray beam between the end of the treatment cone or the port and a distance beyond the chamber equal to at least four times the width of the x-ray beam at the position of the chamber.

3. *The roentgen meter should be carefully placed in position.* The axis of the ionization chamber should be at right-angles to the direction of the x-ray beam. The instrument is intended to measure the exposure (that would obtain in the absence of the instrument) at the point occupied by the center of the thimble ionization chamber. Unless specifically stated otherwise, the exposure is measured at points on the central axis of the x-ray beam.

4. *A correction should be applied when the position of the chamber is displaced from the point where it is desired to measure the exposure rate unless this displacement is less*

*than 1/50 of the distance from the target.* It is often desired to measure the exposure rate at the center of the surface of the composition cover over the aperture of the cone. Since it is impossible to place the roentgen meter with the center of the chamber at the surface of the cover, the following extrapolation method may be used:

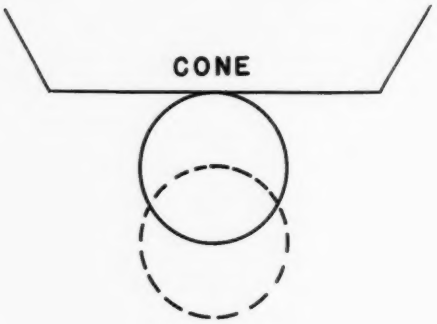


Fig. 2.

Measure the exposure rate with the chamber just below the cover (as the solid circle of Figure 2). Lower the chamber so that the distance from the surface of the cover to the center of the chamber is doubled (dotted circle in figure) and measure the exposure rate in this position. Subtract the second measurement from the first. The result is the correction for the distance from the cover to the center of the chamber. Add this correction to the first reading. (Make sure that the two positions of the chamber lie on the central axis of the x-ray beam.)

Example: First measurement, chamber touching cover—25 r/min.
Second measurement, chamber lowered—21 r/min.
Hence correction for displacement from surface of cone = 25 r/min. − 21 r/min. = 4 r/min.
And exposure rate at surface of cover = 25 r/min. + 4 r/min. = 29 r/min.
The correction may be neglected if the diameter of the chamber is less than 1/25 of the distance from the target and less than 1/10 of the diameter of the field, since the error will probably be less than 5 per cent.

5. *An accurate watch should be used for time measurements.* Do not use a "hand timer" or other time switch for timing exposures when measuring exposure rates. Hand timers are frequently quite inaccurate. Pocket watches are usually more dependable than stop watches and sufficient accuracy is attained if the second hand is read to the nearest second in timing an interval of more than one minute, or within two seconds in an interval of two minutes, etc. Moreover, all measurements intended for future reference should be made after the tube has been in operation for a short time because the output usually changes considerably during the first few minutes of operation. A suitably built-in shutter is the most satisfactory means of controlling the interval during which the roentgen meter is exposed to the x-ray.

## CHAPTER V.—MEASUREMENT OF THE SKIN EXPOSURE

1. *The roentgen meter should be suitable for the quality of x-rays used.* The rays scattered from underlying tissue are softer than the rays received directly from the x-ray tube. Hence the radiation received by the skin, consisting of both primary and scattered radiation, is softer than radiation from the tube in free air. The same caution to verify that the instrument is suitably calibrated as mentioned in the first paragraph of Chapter IV should be observed, and the lower voltage limits therein stated should be raised by 10 kv.

2. *In later treatments the exposed skin should be covered with a sheet of fiber, bakelite, celluloid, wood, or other organic product not containing heavy elements, 1 to 3 mm. thick,* unless the end of the treatment appl cator is permanently closed by a cover of such material. This cover acts as a filter to stop secondary corpuscular rays from the inside of the treatment cone from reaching

the skin. Heavy elements, *e.g.*, lead, lining the treatment cone, may be a source of *additional* corpuscular rays which are not recorded by a properly designed roentgen meter. Since these rays would contribute to the skin reaction they must be excluded to insure a simple and consistent relation between the x-ray exposure and the skin reaction. If an open port without a treatment cone is used, the covering over the skin may be omitted if (1) the potential applied to the tube is less than 400 kv., (2) the width of the exposed area of the skin is greater than 5 cm., and (3) the distance of the skin from metal parts or lead glass parts of the apparatus is at least 5 cm. for 200 kv. or less potential applied to the tube, 10 cm. for 300 kv., and 15 cm. for 400 kv.

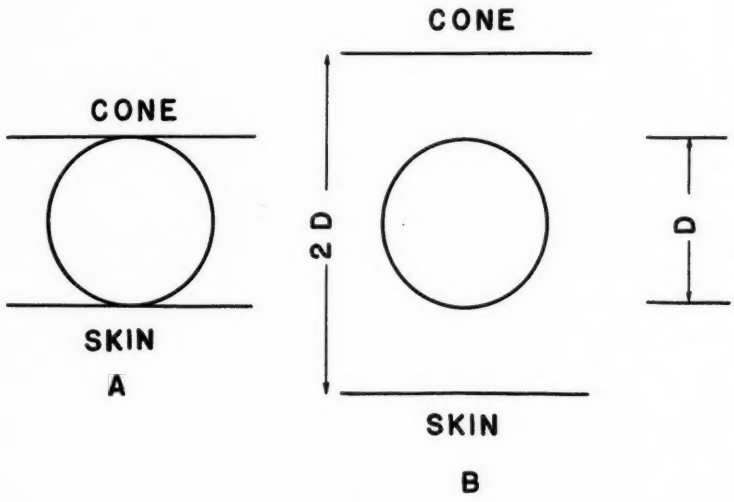


Fig. 3.

3. *Error due to a difference in the position of the chamber of the roentgen meter during measurement and the skin during treatment should be avoided or corrected.* If the chamber of the roentgen meter is placed between the skin and the cover of the treatment cone, it will measure the exposure at a position above the skin a distance equal to half the diameter of the chamber. The error due to this cause is likely to exceed 10 per cent if the width of the field is less than five times the diameter of the chamber. It is usually negligible if the diameter of the chamber is less than 1/50 of the distance from the target and less than 1/15 of the width of the field. The error may be reduced by the following extrapolation method:

Measure the exposure rate with the chamber just touching the skin below, and the applicator cover above (*A*, Fig. 3). Make a second measurement with the center of the chamber separated from the cover above and the skin below by distances equal to the diameter of the chamber (*B*, Fig. 3). (Note that the distances from the surface of the cover to the center of the chamber, and from the surface of the skin to the center of the chamber, are just twice as great as in the first position.) Subtract the second measurement from the first; this will give the approximate correction for the space between the skin and the cone cover. Add this correction to the first reading.[6]

Example: First measurement, position *A*, 20 r/min.
Second measurement, position *B*, 17 r/min.
Hence the correction for the

[6] Care should be taken not to depress the surface of the skin, *e.g.*, by the weight of the chamber.

space is 20 r/min. − 17 r/min. = 3 r/min.

And the approximate exposure rate is 20 r/min. + 3 r/min. = 23 r/min.

A "separator" is useful for adjusting the distances for the second measurement quickly and accurately. This might be a cylindrical ring of bakelite, cardboard, or similar material having a length of twice the diameter of the thimble chamber, and a diameter nearly as large as the applicator cover. A hole in the side wall of the ring permits insertion of the chamber at the correct height. This ring should have a thin wall, so that it scatters little radiation.

*If an open port without treatment cone is used, the error due to the position of the chamber may be reduced by the following extrapolation method:*

Measure the exposure rate with the chamber just touching the skin (solid circle in Fig. 4). Make a second measurement with the *center* of the chamber separated from the skin by a distance equal to the diameter of the chamber (dotted circle).

Fig. 4.

(Note that the chamber is raised a distance of half its diameter for the second measurement, and that the focus–skin distance has not been altered.) Subtract the second reading from the first; this will give the approximate correction for the size of the chamber. Add this correction to the first reading.

Example: First measurement, chamber touching; 20 r/min.

Second measurement, chamber raised 18 r/min.

Hence the correction for the size of the chamber is 20 r/min. − 18 r/min. = 2 r/min.

And the approximate skin exposure rate is 20 r/min. + 2 r/min. = 22 r/min.

4. *An accurate watch should be used for time measurements.* "Hand timers" should not be used. (See Chap. IV, par. 5.)

*The Exit Skin Exposure.*—The exit skin exposure is important in cross-fire treatment methods when the same region of the skin also receives direct exposure. It is always smaller than the direct exposure, and, therefore, need not be determined quite as accurately. For example, if the exit exposure is one-third as great as the direct exposure, three times as large a percentage error may be tolerated in the determination of the exit exposure.

The exit skin exposure may be measured by the methods described above for the skin exposure in direct irradiation. The instrument may be placed against the skin of the exit field. If, for this purpose, it is necessary to place the instrument between the patient's body and the treatment table top, the chamber may be protected from pressure likely to break it by a piece of wood on each side of it. Since less accuracy is required in exit exposure measurements, usually corrections for displacements, as described in Precaution 3 above, are unnecessary.

The exit irradiation depends on the thickness of material close to the skin which is encountered by the radiation after emerging through the exit field, owing to radiation scattered by this material. Care should be taken that the thickness of this material remain unaltered during the measurement and treatment.

## CHAPTER VI.—USE OF "IOMETERS," AND OTHER INSTRUMENTS HAVING IONIZATION CHAMBERS PERMANENTLY INSTALLED IN THE X-RAY APPARATUS, FOR MONITOR PURPOSES

An instrument having an ionization chamber built in the x-ray tube housing or

the treatment cone is a very useful accessory. It informs the radiologist of unpredictable changes in the performance of the x-ray apparatus, which might result in failure to apply the exposure intended.

One type of these instruments has a thimble chamber fixed in the treatment cone, to the window that is pressed against the patient's skin. It is intended to record the skin exposure. Its use is, however, subject to limitations imposed by its immobility, *e.g.*, the difficulty of making correction for the distance between the skin and the center of the chamber as discussed in other chapters.

Other types of these instruments have thimble chambers installed in the tube head above the treatment cone (*e.g.*, the instrument known commercially as the "Iometer"), drum type ionization chambers in the direct beam above the treatment cone, or small ionization chambers mounted outside the direct beam to the patient. These types are monitoring devices only. They do not measure the free air exposure or the skin exposure directly. *Hence they record in arbitrary units—not in roentgens or in roentgens per minute.* Properly used, they help to prevent mistakes in kilovoltage, milliamperage, and filters. They do not, however, give protection against errors in distance.

These monitoring devices are very convenient when determining the skin exposure or the tissue exposure by the use of tables. Thus, the instrument may be "calibrated" in terms of the free air exposure *for the particular choice of conditions to be used* by determining the reading of the instrument which corresponds to a free air exposure rate of 100 r /min. (or, in the case of the recording types, that corresponds to 100 r). The reading of the instrument during treatment, then gives the free air exposure rate, or exposure, and the skin exposure can be calculated by use of the tables.

*Caution: for this purpose the reading of the monitoring instrument should not be affected appreciably by the presence of the patient under the treatment cone.* If its ionization chamber receives radiation scattered from the exposed tissue, a corresponding error will result. This should be tested by observing any sudden change in the reading of the instrument when the patient is removed. If a change of more than 5 per cent is observed, the instrument is not suitable for this purpose. Monitors with drum or plate type chambers are more affected by radiation scattered from the patient than the other types.

In calibrating a monitor instrument in terms of free air exposure rate, the free air exposure should be measured by the methods described in a previous chapter, using a portable dosemeter. Measurements with both instruments should be made concurrently, and, for accuracy, several readings should be taken.

*The calibration applies only to the particular set of conditions under which it was made.* For these conditions the reading of the instrument is proportional to the free air exposure rate at the place for which the calibration is made (*e.g.*, end of the cone). Obviously the free air exposure rate at this place will not retain the same ratio to the reading obtained with an ionization chamber located in another position if the conditions are changed. The calibration is unsatisfactory if the conditions of calibration are departed from by—

(1) Changing the treatment cone.
(2) Changing the metal of the primary filter. (The primary filter is the denser metal when more than one metal is used. The so-called "copper equivalent" of the glass wall of the x-ray tube should not be considered as a part of the filter in this connection, and in condition 3 below.)
(3) Doubling or halving (at least) the primary filter thickness.
(4) Increasing or decreasing the kilovoltage by 20 per cent or more.

Changes within these limits are permissible, without recalibration, if the walls and electrodes of the monitor are of organic material or aluminum. If of denser metals, the filters may not be changed and the kilovoltage must be kept within the limits

of the ordinary power supply fluctuations (*i.e.*, the setting of auto-transformer and rheostat or other kilovoltage control may not be changed).

## CHAPTER VII.—USE OF TABLES TO DETERMINE SKIN EXPOSURE FROM MEASURED FREE AIR EXPOSURE

Table I gives the skin exposure corresponding to 100 roentgens as measured in free air, for several qualities of radiation, for a range of field sizes and body thicknesses, and for various thicknesses of cone cover. The data have been selected because they are applicable to free air exposures measured under the conditions described in Chapter IV. Many similar tables may be found in the literature but they should not be used with free air exposures measured under the conditions and methods of Chapter IV unless it is known that they are applicable.

The increase in the skin exposure as compared to the exposure measured in air depends on four factors: the area of the surface exposed, the quality of the x-rays, the composition and thickness of the cover of the treatment cone, and the depth of tissue and supporting material behind the exposed skin surface. (It is assumed that the support is wood or similar material and no metal is present.) The following precautions should be observed in using the table:

(1) *The free air exposure should be measured by the method described in Chapter IV at the center of the composition cover of the treatment cone, or (in the case of open port treatment without cone) at the same distance in front of the port as the skin is during treatment.*

(2) *If an iometer or other permanently installed ionization chamber is used to indicate the free air exposure, it should be calibrated by the method described in Chapter VI,* in terms of the free air exposure at the position occupied by the skin during treatment, *i.e.*, at the center of the cover of the treatment cone or (in the case of open port treatment) at the center of the beam at the appropriate distance from the port.

(3) *If an iometer or other permanently installed ionization chamber is used to indicate the free air exposure, a test should be made to determine whether or not this instrument receives an appreciable exposure of radiation scattered back from the tissue exposed.* This should be done by removing the patient, or phantom, and other scattering objects and observing whether or not the reading of the instrument differs from the reading obtained before they were removed. If the ionization chamber of the instrument is in the x-ray tube housing above the removable treatment cone (as in the case of the iometer), the difference in the two readings may be negligible unless the cone is short and wide. If the chamber is near the end of the treatment cone, the difference between the two readings may be large, and a correction should be made for it.

*If a difference greater than 3 per cent is found, the dosage rate (or the exposure) indicated by the instrument should be corrected accordingly.*

First example: Reading of iometer with patient exposed, 55 divisions. Reading of iometer with patient removed from x-ray beam, 50 divisions. Previous calibration of the iometer for the particular cone and other conditions used (see Chap. VI) showed that one division of the iometer scale corresponded to 0.400 r/min., hence the free air dosage rate to be used in Table I is $50 \times 0.400$ r/min. $= 20.0$ r/min. The reading of 55 on the iometer is not proportional to the skin exposure, since only a portion of the backscatter is effective in such a chamber. It is simply a monitor reading which must be kept

TABLE I.—SKIN DOSE IN ROENTGENS CORRESPONDING TO 100 ROENTGENS IN AIR AT SAME DISTANCE FROM FOCUS

| Thickness of Underlying Tissue | Open Port | | | | Cover on Treatment Cone 1/8 in. Bakelite | | | | Cover on Treatment Cone 1/4 in. Bakelite | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Irradiated Area (sq. cm.) | | | | Irradiated Area (sq. cm.) | | | | Irradiated Area (sq. cm.) | | | |
| | 5 | 25 | 100 | 400 | 5 | 25 | 100 | 400 | 5 | 25 | 100 | 400 |
| | 120 kv. peak No filter H.V.L. 1.0 mm. Al or 0.035 mm. Cu | | | | | | | | | | | |
| 1 | 104 | 108 | 111 | 113 | 104 | 108 | 111 | 114 | 104 | 109 | 112 | 115 |
| 2 | 107 | 112 | 116 | 119 | 107 | 113 | 117 | 119 | 107 | 113 | 118 | 121 |
| 4 | 110 | 116 | 122 | 125 | 110 | 117 | 123 | 127 | 111 | 117 | 124 | 128 |
| 6 (Max.) | 111 | 117 | 124 | 128 | 111 | 118 | 126 | 130 | 112 | 118 | 127 | 132 |
| | 150 kv. peak 5 mm. Al filter H.V.L. 0.3 mm. Cu | | | | | | | | | | | |
| 1 | 104 | 108 | 112 | 114 | 104 | 108 | 113 | 115 | 104 | 109 | 113 | 116 |
| 2 | 107 | 112 | 118 | 124 | 107 | 113 | 119 | 126 | 107 | 113 | 120 | 127 |
| 4 | 110 | 118 | 126 | 136 | 110 | 119 | 127 | 139 | 111 | 119 | 129 | 142 |
| 7 | 114 | 123 | 134 | 146 | 114 | 124 | 136 | 150 | 115 | 125 | 139 | 154 |
| 12 (Max.) | 115 | 125 | 136 | 150 | 115 | 126 | 138 | 154 | 116 | 127 | 140 | 159 |
| | 200 kv. peak 0.5 mm. Cu filter H.V.L. 0.9 mm. Cu | | | | | | | | | | | |
| 1 | 104 | 107 | 111 | 114 | 104 | 107 | 112 | 115 | 104 | 107 | 112 | 116 |
| 2 | 106 | 112 | 117 | 124 | 106 | 113 | 118 | 126 | 107 | 113 | 119 | 127 |
| 4 | 110 | 117 | 126 | 134 | 110 | 118 | 128 | 137 | 111 | 118 | 129 | 140 |
| 7 | 112 | 122 | 133 | 144 | 112 | 123 | 135 | 148 | 113 | 124 | 138 | 152 |
| 10 | 113 | 123 | 134 | 146 | 113 | 124 | 136 | 150 | 114 | 125 | 139 | 154 |
| 15 (Max.) | 114 | 124 | 136 | 149 | 114 | 125 | 137 | 153 | 115 | 126 | 140 | 158 |
| | 200 kv. peak 2.0 mm. Cu filter H.V.L. 1.8 mm. Cu | | | | | | | | | | | |
| 1 | 102 | 105 | 108 | 110 | 102 | 105 | 109 | 111 | 102 | 105 | 109 | 111 |
| 2 | 104 | 108 | 112 | 117 | 104 | 108 | 113 | 118 | 104 | 109 | 113 | 119 |
| 4 | 106 | 112 | 118 | 125 | 106 | 112 | 119 | 126 | 106 | 113 | 120 | 127 |
| 7 | 108 | 115 | 124 | 132 | 108 | 115 | 125 | 134 | 109 | 116 | 126 | 136 |
| 10 | 108 | 116 | 125 | 134 | 108 | 116 | 126 | 136 | 109 | 117 | 127 | 138 |
| 15 (Max.) | 109 | 117 | 126 | 136 | 109 | 117 | 127 | 139 | 110 | 118 | 128 | 140 |

constant for the set of treatment conditions employed in the particular case under discussion.

Second example: Reading of recording dosemeter with patient exposed, 15 divisions in 60 seconds; reading with patient removed, 15 divisions in 76 seconds. Previous calibration—one division of instrument scale corresponds to 0.82 roentgen. Exposure recorded during the entire treatment—300 divisions. Hence, the total free air exposure to be used with Table I is $300 \times 60\ 76 \times 0.82 = 194$ r.

*It should be noted that a correction determined in this way is applicable only under conditions similar to those under which it is determined, and not with other treatment cones, qualities of x-ray, etc.*

*The Exit Skin Exposure.*—Some difficulty in determining the exit skin exposure by the use of tables results from the fact that it depends on the thickness of other material, such as the top of the treatment table, next the skin, which contributes to

the exposure by back-scatter. This difficulty may be avoided simply by increasing the thickness of the layer of material next the skin by blocks of hard wood or bags of rice and flour to a total of at least 7 cm. When this is done, the skin of the exit field may be regarded as a region in the bulk of the tissue and the exposure may be determined by the method and tables of Chapter IX.

If it is inconvenient or undesirable to place material next the skin of the exit field, approximate values of exit exposures may be obtained from Table IV. Actual exit exposures are given for 5, 10, and 15 cm. thicknesses of part, for several fields, and two qualities of radiation, for cones covered with 1/8 in. bakelite. For other sets of factors, the ratio of the exit exposure to the full thickness exposure can be estimated.

Example: Estimate the exit exposure for a 100 sq. cm. field in a part of the body 7 cm. thick, for 200 kv. x-rays, with a filter of 0.5 mm. Cu and a distance of 50 cm.

The table does not give data for 7 cm. thickness, but this can be estimated from that for 5 and 10 cm. For a 100 sq. cm. field and 5 cm. thickness the exit exposure is 44 per cent; for a full phantom the depth dose at 5 cm. with these factors (see Table II) is 57 per cent. Hence the exit exposure at this level is 44/57 of the dose at the same depth in a complete phantom, or 77 per cent of it. Similarly, for a 10 cm. thickness, the exit exposure is 22/29, or 76 per cent of the dose at the same depth in a complete phantom. Accordingly the exit exposure for a 7 cm. thickness must also be approximately 76 per cent of the dose at the same depth in a complete phantom, which (see above) is 44 per cent. Hence, 76 per cent of 44 or 33 per cent, is the exit exposure desired.

## CHAPTER VIII.—MEASUREMENT OF THE TISSUE EXPOSURE

1. *The roentgen meter should be suitable for the quality of the x-rays measured.* The same precaution should be observed as for the measurement of skin exposure, as discussed in Chap. V, par. 1.

2. *The material used for a phantom should have a specific gravity of 0.95 to 1.0 and contain no chemical element of atomic number greater than 8.* The atomic numbers of the light elements are as follows: H—1, He—2, Li—3, Be—4, B—5, C—6, N—7, O—8. It should contain not more than three atoms of hydrogen for one atom of oxygen in its composition. (Theoretically, the ideal material is one in which

$$(n_1N_1^4 + n_2N_2^4 + \text{etc.})/(n_1N_1 + n_2N_2 + \text{etc.}) = \text{approximately } 400$$

wherein $n_1$, $n_2$, $n_3$, etc., are the relative number of atoms of the elements of atomic numbers, $N_1$, $N_2$, $N_3$, etc., respectively.) This requirement is satisfied by water, and by rice mixed with sufficient flour to fill the spaces between the rice kernels. Hydrocarbons, such as paraffin wax, are not suitable. Wood products that have a specific gravity between 0.95 and 1.00 are satisfactory (*e.g.*, masonite pressdwood).

3. *A roentgen meter with the smallest ionization chamber available should be used.* The air space of the ionization chamber causes less absorption than the phantom material it displaces. Therefore, more primary radiation reaches the center of the chamber and the instrument reads too high. The error due to this cause, when using a chamber 2 cm. in diameter, varies up to 40 per cent depending on depth, with radiation excited at 80 kv. To reduce the error due to the size of the chamber below 10 per cent for radiation of copper half value thickness greater than 0.3 mm., the diameter of the thimble chamber should not be greater than 1 cm.

TABLE II.—TISSUE DOSE IN ROENTGENS CORRESPONDING TO A SKIN SURFACE DOSE OF 100 ROENTGENS, AT 50 CM. FOCUS–SKIN DISTANCE

| Depth (cm.) | Open Port | | | | Cover on Treatment Cone 1/8 in. Bakelite | | | | Cover on Treatment Cone 1/4 in. Bakelite | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Irradiated Area (sq. cm.) | | | | Irradiated Area (sq. cm.) | | | | Irradiated Area (sq. cm.) | | | |
| | 5 | 25 | 100 | 400 | 5 | 25 | 100 | 400 | 5 | 25 | 100 | 400 |
| | 120 kv. peak No filter H.V.L. 1.0 mm. Al or 0.035 mm. Cu | | | | | | | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 56 | 61 | 65 | 68 | 61 | 66 | 69 | 73 | 65 | 68 | 73 | 75 |
| 3 | 26 | 32 | 38 | 43 | 30 | 36 | 41 | 45 | 33 | 38 | 44 | 48 |
| 5 | 14 | 18 | 23 | 27 | 17 | 20 | 26 | 30 | 18 | 21 | 28 | 32 |
| 7 | 8 | 10 | 15 | 19 | 10 | 12 | 17 | 21 | 11 | 13 | 18 | 23 |
| 10 | 4 | 5 | 8 | 12 | 5 | 6 | 9 | 14 | 6 | 7 | 10 | 16 |
| | 150 kv. peak 5 mm. Al filter H.V.L. 0.3 mm. Cu | | | | | | | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 81 | 91 | 96 | 99 | 81 | 90 | 95 | 98 | 81 | 87 | 93 | 95 |
| 3 | 53 | 66 | 77 | 84 | 53 | 63 | 73 | 80 | 53 | 61 | 70 | 77 |
| 5 | 34 | 45 | 56 | 65 | 34 | 44 | 54 | 62 | 34 | 42 | 52 | 60 |
| 7 | 22 | 31 | 41 | 50 | 22 | 30 | 40 | 48 | 22 | 29 | 38 | 47 |
| 10 | 12 | 18 | 26 | 35 | 12 | 17 | 25 | 33 | 12 | 17 | 24 | 32 |
| 12 | 7 | 12 | 19 | 27 | 7 | 11 | 19 | 25 | 7 | 11 | 18 | 25 |
| | 200 kv. peak 0.5 mm. Cu filter H.V.L. 0.9 mm. Cu | | | | | | | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 83 | 93 | 98 | 101 | 82 | 91 | 96 | 98 | 82 | 89 | 94 | 96 |
| 3 | 55 | 70 | 80 | 88 | 55 | 67 | 76 | 84 | 55 | 65 | 73 | 81 |
| 5 | 38 | 49 | 60 | 72 | 37 | 48 | 57 | 68 | 37 | 46 | 55 | 65 |
| 7 | 25 | 35 | 46 | 57 | 25 | 34 | 44 | 54 | 26 | 33 | 42 | 52 |
| 10 | 15 | 21 | 30 | 41 | 15 | 20 | 29 | 38 | 15 | 20 | 27 | 37 |
| 12 | 11 | 15 | 23 | 33 | 11 | 14 | 22 | 31 | 11 | 14 | 21 | 30 |
| 15 | 5 | 9 | 16 | 22 | 5 | 8 | 15 | 21 | 5 | 8 | 15 | 20 |
| 20 | 3 | 4 | 8 | 11 | 3 | 4 | 8 | 10 | 3 | 4 | 8 | 10 |
| | 200 kv. peak 2.0 mm. Cu filter H.V.L. 1.8 mm. Cu | | | | | | | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 83 | 93 | 98 | 101 | 83 | 91 | 96 | 99 | 83 | 90 | 94 | 97 |
| 3 | 56 | 71 | 81 | 89 | 57 | 68 | 78 | 85 | 57 | 65 | 75 | 82 |
| 5 | 39 | 51 | 63 | 74 | 39 | 49 | 60 | 70 | 38 | 48 | 58 | 67 |
| 7 | 26 | 37 | 48 | 59 | 26 | 36 | 46 | 57 | 27 | 35 | 45 | 54 |
| 10 | 16 | 23 | 34 | 44 | 16 | 22 | 32 | 42 | 17 | 22 | 31 | 41 |
| 12 | 12 | 17 | 27 | 36 | 12 | 16 | 26 | 35 | 12 | 16 | 25 | 34 |
| 15 | 6 | 11 | 19 | 25 | 6 | 10 | 19 | 24 | 6 | 10 | 18 | 24 |
| 20 | 3 | 5 | 9 | 14 | 3 | 5 | 9 | 13 | 3 | 5 | 9 | 13 |

4. If the tissue exposure is to be evaluated as a percentage of the free air exposure, of the skin exposure, or in terms of the reading of a monitor, *the free air exposure, skin exposure, or monitor reading should be measured by the methods described in this bulletin.* The most common practice is to express tissue exposure as a percentage of the skin exposure.

5. Unless otherwise specifically stated, tissue exposures are measured at points along the central axis of the x-ray beam.

6. The tissue exposure having been determined by previous measurements with the phantom, *the following conditions should be closely reproduced* in using the data for actual treatment: *kilovoltage, filtration, focus–skin distance,* skin *area* exposed, *depth* of tissue, and other material directly below skin surface and the *density* of these materials. A new calibration should be made if the conditions are altered by—

(1) Changing the treatment cone,
(2) Changing the metal of the filter,
(3) Changing the thickness of the primary (more dense) filter by more than 20 per cent (ignore so-called

"copper equivalent" of tube wall and oil),

(4) Changing the kilovoltage by more than 15 per cent.

Tissue exposure measurements made in phantoms as described above are directly applicable for treatment in regions containing predominantly muscle or connective tissue. Owing to differences in density and atomic composition, they differ slightly from the true tissue exposure in regions containing predominantly bone, cartilage, or lung tissue. If the tissue exposure is desired in a part of the body such that the thickness of material beyond the point in question (including wood or other support behind the exposed part of the body) is less than 7 cm., measurements must be made in a phantom of proper size, or a correction must be made to values obtained in a large phantom. The latter method will be discussed in the next chapter.

7. *Measurements of time should be made with a watch.* Hand timers and other automatic switching devices should not be used. (See Chap. IV, par. 5.)

## CHAPTER IX.—USE OF TABLES TO DETERMINE THE TISSUE EXPOSURE FROM SKIN EXPOSURE

Table II gives the tissue exposure corresponding to a skin surface exposure of 100 roentgens, for a wide range of qualities of radiation and of field sizes. The data have been selected because they are applicable to surface dosage measured by the method described in Chapter V. Similar tables may be found in the literature, but they should not be used with skin surface dosages measured by the methods of Chapter V unless it is known that they are applicable.

The difference between the tissue exposure and the skin exposure depends on six factors: the depth below the skin surface, the thickness and composition of the treatment applicator cover, the quality of the x-rays, the thickness of tissues and support directly below the skin, the area of the skin surface exposed, and the target–skin distance.

The skin exposure, from which the tissue exposure is to be determined by the use of tables, may be measured by the method of Chapter V, or determined from the measured exposure in free air by the tables of Chapter VII.

The following precautions should be observed in using the tables:

(1) *The skin exposure should be measured by the methods described in Chapter V, or determined from the free air exposure by the tables of Chapter VI,* and corrected to apply to the skin in contact with the applicator cover. Otherwise the data will not be applicable. The skin exposure should be determined at the center of the exposed field.

(2) *If an iometer or other type of monitor ionization chamber is used to indicate skin exposure, the monitor should be calibrated by the method described in Chapter VI.*

(3) *Correction should be made to the tissue exposure obtained from Table II if the target–skin distance differs from 50 cm.* Table II gives the tissue exposure for a target–skin distance of 50 cm. For other target–skin distances correct by multiplying the value obtained from Table II by the factors given in Table III.

Example: Using x-rays generated at 200 kv. peak, having a h.v.l. of 1.8 mm. Cu, at a distance of 70 cm., and with a field of 200 sq. cm., the cover on the treatment cone being 1/8 in. bakelite, find the roentgens delivered at a depth of 12 cm. per 100 r on the skin. This field size is not included in the tables; it is necessary to interpolate. From Table II, for this quality of radiation and this cone cover, for 100 r on surface, with 50 cm. target–skin distance, at 12 cm. depth in

100 sq. cm. field—26 r;
400 sq. cm. field—35 r.

This is a difference of 35 − 26

TABLE III.—FACTORS FOR DETERMINING DEPTH DOSES AT VARIOUS FOCUS–SKIN DISTANCES IN TERMS OF EACH DEPTH DOSE FOR 50 CM. DISTANCE AS 100 PER CENT, SKIN DOSE 100 PER CENT FOR EVERY DISTANCE

| Depth (cm.) | Focus–skin Distance (cm.) | | | | | |
|---|---|---|---|---|---|---|
| | 30 | 40 | 50 | 70 | 100 | 150 |
| | Percentage of Depth Dose at 50 cm. | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 97.5 | 99.0 | 100 | 101 | 102 | 103 |
| 2 | 95.5 | 98.0 | 100 | 102 | 104 | 105 |
| 3 | 93.2 | 97.5 | 100 | 103 | 106 | 108 |
| 5 | 89.2 | 95.5 | 100 | 106 | 110 | 114 |
| 7 | 85.5 | 94.2 | 100 | 108 | 114 | 119 |
| 10 | 81.2 | 92.3 | 100 | 110 | 118 | 126 |
| 12 | 78.5 | 91.0 | 100 | 112 | 122 | 133 |
| 15 | 75.5 | 89.8 | 100 | 115 | 127 | 140 |
| 20 | 70.5 | 87.4 | 100 | 119 | 136 | 153 |

= 9 r for a difference of 300 sq. cm. For a difference of 100 sq. cm., the difference in exposure would be about one-third as great, or 3 r. Hence, at 50 cm. distance the depth dose is

26 r + 3 r = 29 r per 100 r on the skin.

From Table III it is found that at 12 cm. depth the dose with a 70 cm. distance is 112 per cent of that with 50 cm. distance.

112 per cent of 29 r = 32 r per 100 r on the skin.

It should be pointed out that the inverse square law holds only for point sources of radiation. For positions close to the filter or tube holder, deviations may be considerable. Exposure data for such positions must be determined by special calibrations rather than by attempting to correct tables of values obtained at longer distances.

(4) *Errors due to insufficient depth of underlying tissue should be avoided.* The data given in Table II have been determined by the use of a very deep phantom. They are directly applicable for the determination of the exposure in very thick parts of the body, except within a few centimeters of the skin surface where the rays emerge on the side of the body remote from the x-ray tube (*i.e.*, the "exit field"). Owing to the small thickness of the material contributing to the back-scattering in this region close to the exit field, the exposure is smaller than that given in the table. This difficulty is particularly important in the treatment of thinner parts of the body. Significant errors due to this cause may be avoided either by applying corrections or by providing a layer of suitable material over the exit field.

The second alternative, that of providing a layer of material behind the exposed part of the body, is much simpler than the other and has the additional advantage of increasing the depth dose. It has, however, the disadvantage of increasing the exit exposure. Blocks of hardwood or bags of rice may be used for this purpose. The total thickness of material (including tissue, the additional material provided, the mattress and wood top of the treatment table immediately underneath) in the x-ray beam beyond the place at which the dose is to be determined, should be at least 8 cm. Under these conditions, the data given in this chapter are applicable without corrections for errors due to lack of underlying scattering material.

TABLE IV.—DEPTH AND EXIT DOSES IN PHANTOMS OF LIMITED THICKNESSES: TISSUE DOSES CORRESPONDING TO A SKIN SURFACE DOSE OF 100 ROENTGENS 200 KV. PEAK. 50 CM. FOCUS–SKIN DISTANCE. COVER ON TREATMENT CONE 1/8 IN. BAKELITE

| Depth (cm.) | Irradiated Area 5 sq. cm. | | | Irradiated Area 25 sq. cm. | | | Irradiated Area 100 sq. cm. | | | Irradiated Area 400 sq. cm. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Thickness of Part (cm.) | | | Thickness of Part (cm.) | | | Thickness of Part (cm.) | | | Thickness of Part (cm.) | | |
| | 5 | 10 | 15 | 5 | 10 | 15 | 5 | 10 | 15 | 5 | 10 | 15 |
| | 0.5 mm. Cu filter H.V.L. 0.9 mm. Cu | | | | | | | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 80 | 82 | 82 | 87 | 91 | 91 | 90 | 96 | 96 | | 98 | 98 |
| 3 | 51 | 55 | 55 | 62 | 67 | 67 | 68 | 75 | 76 | | 82 | 84 |
| 5 | 34 | 37 | 37 | 41 | 47 | 48 | 44 | 55 | 57 | | 64 | 68 |
| 7 | | 24 | 25 | | 33 | 34 | | 41 | 43 | | 48 | 52 |
| 10 | | 13 | 15 | | 16 | 20 | | 22 | 28 | | 27 | 36 |
| 12 | | | 11 | | | 13 | | | 20 | | | 27 |
| 15 | | | 4 | | | 6 | | | 11 | | | 15 |
| | 2.0 mm. Cu filter H.V.L. 1.8 mm. Cu | | | | | | | | | | | |
| 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 1 | 81 | 83 | 83 | 87 | 91 | 91 | 90 | 96 | 96 | | 99 | 99 |
| 3 | 53 | 57 | 57 | 63 | 68 | 68 | 70 | 77 | 78 | | 83 | 85 |
| 5 | 36 | 39 | 39 | 42 | 48 | 49 | 46 | 58 | 60 | | 66 | 70 |
| 7 | | 25 | 26 | | 35 | 36 | | 43 | 45 | | 50 | 55 |
| 10 | | 13 | 16 | | 18 | 22 | | 25 | 31 | | 30 | 40 |
| 12 | | | 12 | | | 15 | | | 24 | | | 31 |
| 15 | | | 5 | | | 8 | | | 13 | | | 17 |

The first alternative method, that of applying corrections to avoid error due to this cause, is more difficult owing to the number of conditions which must be considered. Approximate values of exposures with small thicknesses of underlying material may be obtained from Table IV. Actual depth dose data are given for 5, 10, and 15 cm. thick phantoms. By comparing these values with those for thick phantoms, in Table II, one sees what portion of the tabulated dose is due to the back-scatter from the extra layers, and can make this calculated reduction in the case when the extra layers are not there.

Example: With x-rays generated at 200 kv., 0.5 mm. Cu filter, 50 cm. distance, 25 sq. cm. field, 1/8 in. bakelite cover, estimate the exposure at a depth of 10 cm. in a neck 12 cm. in diameter. From Table II, the exposure at this depth in a full phantom is 20 r per 100 r on the skin. To obtain an idea of the reduction necessary, find a place in Table IV for the same field and quality of radiation, where the exposure is given for a position such that about the same thickness of tissue (2 cm.) exists beyond the point of measurement. The exposure at 12 cm. in a phantom 15 cm. thick should serve. This is 13 r per 100 r on the skin. For the thick phantom the dose at the same depth is 14 r. Hence an approximation to the exposure desired should be 13/14 of 20, or 18.6 r per 100 r on the skin. This is still slightly high because the values from Table IV were for 3 cm. of tissue beyond the point, while in the problematical case there are only 2 cm. Hence the exposure can be taken as 18 r per 100 r on the skin, as a satisfactory approximation.

TABLE V.—TISSUE DOSE IN ROENTGENS CORRESPONDING TO A FREE AIR DOSE OF 100 ROENTGENS AT 50 CM. FOCUS–SKIN DISTANCE

| Depth (cm.) | Open Port | | | | Cover on Treatment Cone 1/8 in. Bakelite | | | | Cover on Treatment Cone 1/4 in. Bakelite | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Irradiated Area (sq. cm.) | | | | Irradiated Area (sq. cm.) | | | | Irradiated Area (sq. cm.) | | | |
| | 5 | 25 | 100 | 400 | 5 | 25 | 100 | 400 | 5 | 25 | 100 | 400 |
| | 200 kv. peak 0.5 mm. Cu filter H.V.L. 0.9 mm. Cu | | | | | | | | | | | |
| 0 | 114 | 124 | 136 | 149 | 114 | 125 | 138 | 153 | 115 | 126 | 141 | 158 |
| 1 | 95 | 115 | 133 | 150 | 95 | 114 | 132 | 150 | 94 | 111 | 133 | 152 |
| 3 | 63 | 87 | 109 | 131 | 63 | 84 | 105 | 129 | 63 | 82 | 103 | 128 |
| 5 | 43 | 61 | 82 | 107 | 43 | 60 | 77 | 104 | 43 | 58 | 77 | 103 |
| 7 | 29 | 43 | 63 | 85 | 29 | 42 | 61 | 83 | 29 | 42 | 59 | 82 |
| 10 | 17 | 26 | 41 | 61 | 17 | 25 | 40 | 58 | 17 | 25 | 39 | 58 |
| 12 | 13 | 20 | 33 | 50 | 13 | 18 | 30 | 48 | 12 | 18 | 30 | 48 |
| 15 | 6 | 11 | 22 | 33 | 6 | 10 | 21 | 32 | 6 | 10 | 21 | 32 |
| 20 | 3 | 5 | 11 | 15 | 3 | 5 | 11 | 15 | 3 | 5 | 11 | 16 |
| | 200 kv. peak 2.0 mm. Cu filter H.V.L. 1.8 mm. Cu | | | | | | | | | | | |
| 0 | 109 | 117 | 126 | 136 | 109 | 117 | 127 | 138 | 110 | 118 | 128 | 139 |
| 1 | 90 | 109 | 124 | 137 | 91 | 107 | 122 | 137 | 91 | 106 | 120 | 135 |
| 3 | 61 | 82 | 102 | 121 | 62 | 80 | 90 | 117 | 63 | 77 | 96 | 114 |
| 5 | 42 | 60 | 79 | 101 | 42 | 50 | 76 | 97 | 42 | 57 | 74 | 93 |
| 7 | 28 | 43 | 60 | 80 | 28 | 42 | 58 | 79 | 29 | 41 | 57 | 75 |
| 10 | 17 | 27 | 43 | 60 | 17 | 26 | 41 | 58 | 19 | 26 | 40 | 57 |
| 12 | 13 | 20 | 34 | 50 | 13 | 19 | 33 | 48 | 13 | 19 | 32 | 47 |
| 15 | 7 | 13 | 24 | 34 | 7 | 12 | 24 | 34 | 7 | 12 | 23 | 35 |
| 20 | 3 | 6 | 11 | 19 | 3 | 6 | 11 | 18 | 3 | 6 | 11 | 18 |

## CHAPTER X.—USE OF TABLES TO DETERMINE THE TISSUE EXPOSURE FROM THE FREE AIR EXPOSURE

Table V gives the tissue exposure at various depths, corresponding to an exposure *in free air* of 100 roentgens, at the position of the skin surface. It has been compiled from the same data as the tables in Chapters VII and IX. The table applies only to a limited number of conditions, *i.e.*, 50 cm. focus–skin distance, 0.9 and 1.8 mm. Cu h.v.l., covers of 0, 1/8 in. and 1/4 in. bakelite on the treatment cones, and 5, 25, 100, and 400 sq. cm. fields. These conditions are, however, frequently employed in therapy at the present time.

A comprehensive table applicable to all conditions likely to be used would be difficult to prepare and inconveniently lengthy, owing to the large number of conditions that affect the tissue exposure. If it is desired to determine the tissue exposure from the free air exposure for a set of conditions not included in Table V, this may be done in two steps, *viz.*, by (first) obtaining the skin dose from the free air exposure by the method of Chapter VII, and (second) using the skin exposure so obtained to determine the tissue exposure by the method of Chapter IX.

If a particular set of conditions that is not included in Table V is used frequently, the radiologist will find it convenient to prepare a suitable table on the same principles as Table V. For example, the data for 50 cm. focus–skin distance, 1/4 in. bakelite cover, 400 sq. cm. field, 0.9 mm. Cu h.v.l., which are given in the right-hand column of Table V, were obtained by the following method: From Table I it is seen that, for the above conditions, a free air exposure of 100 r is equivalent to a skin exposure on a large phantom of 158 r. Multiplying the depth doses in Table II by the ratio of these (1.58) gives the desired table of depth exposures as percentages of free air exposures *for the same physical factors*.

The table thus prepared is applicable to a focus–skin distance of 50 cm. For any other distance an additional step in the calculations is required; the values obtained by the above calculations must be

multiplied by the percentages given in Table III for the desired distance.

Tissue exposures determined from Table V, or from tables suited to particular conditions as suggested above, may be in error due to a shallow depth of underlying tissue. (See Chapter IX, recommendation 4.)

## GLOSSARY

Absorption:[7] Attenuation of a beam of x-rays when traversing matter, by deflection of part of the rays from the original direction of propagation, and by the conversion of the energy of part of the rays into other forms of energy, such as motion of ions, etc. (The word is also used to mean these two processes that cause the attenuation.)

Absorption Curve: Curve showing percentage of radiation remaining after the beam traverses increasing thickness of a particular substance. (More appropriately called "transmission curve.")

Ångstrom (Å.): Unit of length for defining visible light and x-rays, equal to one ten-millionth of a millimeter.

Atomic Number (At. No.): Number expressing net positive charge on nucleus, or number of orbital electrons, in the neutral atom.

Atomic Weight (At. Wt.): Weight of atom, in terms of weight of oxygen as 16.

Back-scatter: Radiation scattered backward within a volume of matter and re-emerging through the area of incidence.

Calibration: Comparison of a practical measuring instrument or device with another which is known to read correctly. Calibration of x-ray roentgen meters may be done at the National Bureau of Standards (Washington, D. C.), the National Research Council of Canada, or certain officially recognized private laboratories.

Corpuscular Rays: Sub-atomic particles travelling at very high velocities; beta rays, cathode rays, protons, deuterons, alpha rays, neutrons.

Corpuscular Rays, Secondary: Electrons released at very high velocities in consequence of absorbing energy from x-rays.

Depth Dose: Dose at specified depth below the surface of the body (or phantom).

Diaphragm: Aperture, usually variable in size, through which x-rays emerge from tube holder.

Dosage Rate: *See* Exposure rate.

Dose: *See* Exposure.

Dose Meter: *See* Roentgen meter.

Dose Meter, Integrating: A dose or roentgen meter which determines the total exposure during a treatment.

Effective Wave Length: ($\lambda$ Eff.) Wave length of monochromatic radiation which would be absorbed in a specified substance at the same rate as the heterogeneous beam under consideration.

Electrode: Electrically charged terminal in x-ray tube or ionization chamber.

Electrometer: An instrument for measuring differences in potential, applicable with accessories for measurement of very small currents.

Electron: Sub-atomic particle having negative charge of electricity; the natural elementary quantity of negative electricity.

Electron, Photo: Electron set into swift motion by the impact of a photon; the photon gives up all of its energy and ceases to exist.

Electron, Recoil (or Compton): Electron set into motion by impact of a photon; the photon loses only a part of its energy.

Electrostatic Unit of Charge (E.S.U.): The quantity of electricity which repels an equal and similar quantity at a distance of one centimeter in a vacuum with a force of one dyne (2,095,000 times the charge on an electron).

Electrostatic Unit of Current: The passage of one electrostatic unit of charge per second ($3.33 \times 10^{-10}$ amperes).

Exit Skin Dose (or Exposure): The skin dose or exposure in the exit field. *See* Skin dose.

Exposure; Dose: A physical quantity, expressed in roentgens, associated with the radiation traversing a specified point during a specified time, treatment, or act of irradiation. The number of roentgens that would be recorded by a standard ionization chamber traversed by photons identical in quality and number per unit cross sectional area with those traversing the specified point in the specified act of irradiation.

Exposure Meter: *See* Roentgen meter.

Exposure Rate: Dosage Rate: The exposure per unit time.

Extra-hard Radiation: X-rays generated with more than 250 kv. applied to the x-ray tube, and filtered by at least 0.5 mm. Cu or the equivalent. X-rays of h.v.l. more than 3 mm. Cu.

Field: The area on the skin through which a given beam of radiation passes.

Filter: Any substance interposed in a beam of radiation for the purpose of changing its quality.

Filter, Composite: A filter of three or more metals of different atomic numbers (the highest being the primary filter).

Filter, Primary: The filter employed to produce the desired effect on the primary beam.

Filter, Secondary: The material inserted between the primary filter and the patient to absorb the soft secondary radiation from the primary filter.

Filter, Thoraeus: A composite filter of tin, copper, and aluminum.

Filtration: Changing the quality of a beam of radiation (usually to make it more penetrating) by passing it through a layer of material.

Focal Skin Distance: Distance from focal spot of x-ray tube to skin of patient.

Free Air Dose: *See* Free air exposure.

Free Air Exposure: Exposure in air when the scattered radiation is negligible.

Frequency: Number of cycles or complete oscillations per second. (Denoted by Greek letter $\nu$, nu.)

Half Value Layer (h.v.l.): Thickness of material which reduces to half the intensity of a particular beam of radiation.

Hard X-rays: X-rays of short wave length or large half value layer; penetrating x-rays.

Heterogeneous Radiation: A beam of radiation containing a mixture of many wave lengths.

Homogeneous Radiation: A beam of radiation of a single wave length.

Intensity: Dose or exposure per unit time.

Inverse Square Law: Statement of the diminution of radiation from a point source with distance from the source. The intensity of radiation at any point varies inversely as the square of the distance from the point source, provided there is negligible absorption in the intervening space.

Iometer: Trade name of a particular type of monitor ionization chamber (q.v.).

Ion: Charged particle. The fundamental part of the negative ion is an electron; of the positive ion an atom from which an orbital electron has been removed. Either of these particles may attach itself

[7] Absorption, as defined here, is often called "total absorption," as it is sometimes desirable to distinguish the parts of the absorption due to the different processes that contribute to it.

to a group of molecules, in which case the whole group becomes the ion.

Ionization: Breaking the neutral, normal atom or molecule into ions, usually by the action of radiation.

Ionization Chamber: Device for collecting ions produced in a definite region in the beam of radiation. When it is suitably attached to a proper measuring instrument, this affords a measure of the exposure or dose.

Ionization Chamber, Air Wall: A chamber with walls of material of low atomic number, having the same effective atomic number as atmospheric air.

Ionization Chamber, Extrapolation: An ionization chamber arranged so that the enclosed air volume may be altered and reduced almost to zero.

Ionization Chamber, Thimble: Small enclosed ionization chamber having a volume usually less than two cubic centimeters.

Ionization Chamber, Thin Wall: An ionization chamber having walls so thin that nearly all secondary corpuscular rays reaching them from external materials can penetrate them easily.

Ionization Chamber, Standard: An ionization chamber so designed, with due regard to the definition of the roentgen, that dose may be determined by calculation from the electric charge accumulated during irradiation.

Irradiation: Act of administering radiation.

Monitor Ionization Chamber: An ionization chamber used for checking the constancy of performance of the x-ray apparatus.

Monochromatic Radiation: Radiation of a single wave length. (Homogeneous.)

Neutron: Sub-atomic particle having no electric charge, and mass approximately equal to that of the hydrogen atom.

Percentage Depth Dose: Amount of radiation delivered at a specified depth in tissues in percentage of that delivered at the center of the skin field.

Phantom: Volume of material, usually water or some organic substance, used as a substitute for the human body in experimental studies of distribution of radiation.

Port: The aperture in the tube holder through which the beam emerges. *See* Diaphragm.

Port, Open: Omission of cones or applicators between the port and the skin field.

Photon: A single ray (*e.g.*, x- or gamma-ray). The quantity of radiant energy involved in a single process when the radiation acts on an atom or atomic particle.

Primary Radiation: Radiation received directly from the focal spot of the tube.

Quality: The property of the radiation which determines the manner in which it affects and is altered by the matter it traverses, expressed quantitatively in terms of wave length (q.v.) or half value layer (q.v.).

Quantum: Amount of energy associated with a photon; the x-ray energy reacting with or affecting a single atom or ion.

Recombination: Reunion of positive and negative ions to form neutral atoms.

Roentgen (r): Unit of dose or exposure of x-radiation. The quantity of x- or gamma-radiation such that the associated corpuscular emission per 0.001293 gram of air produces, in air, ions carrying 1 e.s.u. of quantity of electricity of either sign.

Roentgen Meter: An instrument for measuring exposure, usually by ionization methods.

Saturation Current: Current that would be obtained from an ionization chamber if all ions formed by the radiation were utilized.

Saturation Voltage: Voltage on ionization chamber necessary to obtain almost saturation current.

Scattering: Change in direction, and (usually) quality of radiation in passing through matter.

Scattered Radiation: Radiation whose direction has been changed and (usually) quality altered by collisions with atoms of material.

Secondary Radiation: Radiation generated in atoms of material by impact of electrons or photons.

Soft X-rays: X-rays of long wave length or low half value layer; x-rays which can be easily absorbed.

Supervoltage: Voltage greater than 250 kilovolts.

Skin Exposure; Skin Dose: Exposure or dose at skin surface.

Target–skin Distance: Distance from center of focal spot of target to center of irradiated area on skin.

Timer: Instrument for measuring the duration of irradiation.

Tissue Exposure; Tissue Dose: Exposure or dose at specified point in tissue.

Total Radiation: Sum of primary, scattered, and secondary radiation.

Treatment Applicator; Treatment Cone: Device inserted into port to define beam of rays at skin field and establish correct target–skin distance.

Wave Length: A quantity (with the dimensions of length) used to specify the quality of x-rays.

X-radiation, Characteristic: X-radiation of quality determined by, and characteristic of, material in which it is generated.

X-radiation, Fluorescent: Characteristic x-radiation.

X-radiation, Continuous Spectrum: X-radiation emitted by the x-ray tube which is not characteristic radiation.

X-ray Spectrum: Radiation distributed or sorted out according to quality.

X Unit: 0.001 Ångstrom.

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# FAMILIAL LUMBOSACRAL SYRINGOMYELIA[1]

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THE appearance in our clinic of two or more members of four different families with trophic changes in the soft and bony tissues of the feet has led us to review the literature of similar cases. One of our cases was sporadic, but as the picture was similar to the familial cases we have included it in our report—all the more so since one case, at first considered sporadic, was found to be one of seven in the family.

We have hesitated long as to the proper title to use. It is our belief that the various etiologic factors of the syndrome are of the developmental type and that the terms, *status dysraphicus*, *myelodysplasia*, *syringomyelia*, and *trophopathia pedis myelodysplastica*, all have some basis for being suggested as the preferable term.

Since there is no reported autopsy on a case of this type, except one incomplete report by Schlesinger on the case of Verhoogen and Vandervelde (65) and considered by him not to be syringomyelia, the choice of a term rests almost entirely on a clinical basis.

Status dysraphicus (Bremer, 7) is especially frequent in relatives of persons with syringomyelia. He found that spinal cords of persons with funnel chest revealed gliotic changes around the central canal in six of eight cases, these changes differing in degree but not in nature from those found in syringomyelia.

The most striking and frequent manifestations of status dysraphicus are anomalies of the sternum, kyphoscoliosis, differences in the mammary glands, body span exceeding body length, livid cold hands, tendency to bending or curvature of the fingers, disturbances of sensation of circular limitation, and nocturnal enuresis.

Myelodysplasia (Fuchs, 17) is characterized by syndactyly, dissociated sensory loss, open sacral canal, anomalies of the superficial and deep reflexes of the abdomen and legs, deformities of the feet often with peroneal weakness and trophic and vasomotor disturbances of the feet.

*Trophopathia pedis Myelodysplastica.*—Under this title Kienböck (31) has reported four sporadic cases, in three of which the changes in the feet closely resembled those in our series. In only one case was a radiograph made of the spine and this showed a spina bifida. He collected 17 cases of occult spina bifida with trophic changes in the skin and bones of the feet and classified his cases among that group.

There exists a closely allied group of cases with symmetrical gangrene of the hands and feet (Table I). Of these, 18 familial and one sporadic case have been reported. The largest series was one of eight cases reported by Nékám (44).

TABLE I

| | Familial | Sporadic |
|---|---|---|
| Grossoni | | 1 |
| Guillain and Thévenard | 2 | |
| Nékám | 8 | |
| Price | 3 | |
| Halliday and Whiting | 5 | |
| Total | 18 | 1 |

Syringomyelia rarely occurs as a familial disease, only 44 cases being recorded in which the distribution was of the usual cervico-thoracic type (Table II). In only four families did the number of cases exceed two. The exceptional series was one of 13 cases reported by Barraquer and de Gispert (4). These authors examined five

[1] Presented before the Fifth International Congress of Radiology, at Chicago, Sept. 13–17, 1937.

cases and had a history of eight others. They were, however, quite different from the classical type of syringomyelia and from the reported cases of symmetrical gangrene of the hands and feet, representing rather a mixture of the two conditions.

TABLE II

| | Number of Cases |
|---|---|
| Barraquer and de Gispert | 13 |
| Barré and Réys | 2 |
| Goldbladt | 2 |
| Karplus | 2 |
| Kino | 4 |
| Krukowski | 2 |
| Mankowsky and Czerni | 4 |
| Nalbaudoff | 2 |
| Preobajenski | 3 |
| Redlich | 2 |
| Sindelar | 2 |
| Tenner | 2 |
| Van Bogaert | 2 |
| Wexberg | 2 |
| Total | 44 |

In general we have classified our cases in the syringomyelia group, and we feel that the term "familial lumbosacral syringomyelia" is the best one for their designation.

*Familial Lumbosacral Syringomyelia.*—To date, there have been reported 54 cases, to which we are now adding 27 of our own, making a total of 81 cases in all. Of these, 71 are familial and 10 sporadic (Table III).

The typical case begins in the 'teens with calluses on the soles of the feet. These ulcerate and heal slowly—if at all. The process is usually painless in the absence of extensive infection, and the patient is rarely obliged to remain off his feet. The toes become discolored, swollen or shrunken, and are removed piecemeal. The metatarsal bones later undergo the same process. Infection may necessitate incision and pieces of bone may be discharged.

The feet become increasingly deformed through scarring of the soft tissues and loss of bone. In cases of extensive infection, amputation may be required. Several patients have died of infection. Rarely does the process extend above the ankle.

The general health is good, the sphincters and sexual life remain normal, and there is surprisingly little interference with the patient's activity and work, even though it requires him to be upon his feet all day.

By the family, the condition is usually attributed to freezing of the feet or to some trauma. In one case the feet were deformed at birth (pes cavus), but the later developments were typical. In a second case the right foot was clubbed at birth. This patient is now three years of age. Under treatment, the child has good use of the foot and there has been nothing unusual in its course, but it is included in this series because, with a history of six other cases in the family, it is felt that this child will almost certainly develop the syndrome later in life. In a third case the patient had always walked on the balls of his feet and had been somewhat awkward. In two cases the condition was attributed by the patients (sisters) to an attack of meningitis at the ages of three and four years, respectively.

TABLE III

| | Number of Cases | |
|---|---|---|
| | Familial | Sporadic |
| Bruns | 3 | |
| Chavany and Thiébaut | | 2 |
| Clarke and Groves | 2 | |
| Foor, Allen, and Morton | | 1 |
| Göbell and Runge | 13 | |
| Guillain and Dubois | | 1 |
| Guillain, Mathieu, and Lereboullet | | 1 |
| Guillain and Thévenard | 2 | |
| Kienböck | | 3 |
| Mertens | | 1 |
| Oehlecker | 2 | |
| Riley | 7 | |
| Schultz | 3 | |
| Smith | 6 | |
| Thévenard and Coste | 2 | |
| Van Epps and Kerr | 26 | 1 |
| Verhoogen and Vandervelde | 3 | |
| Wagner | 2 | |
| Total | 71 | 10 |

### TYPICAL CASE HISTORIES

Case 1. E. J. (K 3199), white, male, married, aged 41 years, was admitted to the University Hospital on Aug. 20, 1934. He has three children, two of whom appear

normal, but one child aged 17 (I. J.) has abnormal feet.

*Family History.*—Mother, brother, two sisters, one nephew, and one son all have foot trouble.

*Past Medical History.*—Negative.

*Present Illness.*—Began at the age of 19 years with an ulcer on the ball of the left great toe. This healed in six months to reopen five years later, since when it has been present most of the time. On several occasions pieces of bone have been discharged. When enlarging, the ulcers are painful. During the last ten years the left foot has become much shorter. At the age of 37 similar ulcers appeared on the right foot. At times the toes would become very tender and glands would appear in the groin, but the patient has never had any fever. He had never noted any loss of sensation in his feet until it was discovered at the hospital. His general health is good and bowel and bladder functions are normal. The urine has been repeatedly examined for sugar with negative results. The general examination is negative except for the legs. The laboratory tests—blood, urine, Wassermann reactions, and spinal fluid—are all normal. Both feet are deformed, especially the left, which is shortened and discolored. On the left sole are two ulcers at the base of the first and third toes. On the dorsum are scars of former ulcers. On the ball of the right foot are the scars of former ulcers. The strength of the legs and toes is normal throughout. Knee-jerks, 3+/3+; tendo-achilles, 1+/1+; plantars extension/extension; ankle clonus 6/−. Sensation is intact over the shins. On the feet, pallesthesia and pain sensation are absent and light touch is only 25 per cent. The station is normal. The gait is somewhat wide and careful.

*Roentgen Examination.*—Dorso-plantar and oblique films of both feet show marked shortening and atrophic changes involving the distal ends of all the metatarsals and proximal phalanges of the left foot. There is roughening and some spicule formation. The metatarso-phalangeal joints are completely disorganized and the distal phalanges are either missing or are markedly atrophic. The right foot shows similar changes, but to a less marked degree, the main change in this foot being in the first metatarso-phalangeal joint and the distal phalanges. There is nothing to suggest osteomyelitis. The bilateral involvement, with uniform changes in the bones of each foot, makes us feel that we are dealing with a trophic lesion of long

Fig. 1.

Fig. 2-*A*.

Fig. 1. E. J., male, aged 41 years. This is our first recognized case, as well as the first case of the "J" family. The patient's main complaint was deformed feet with plantar ulcers. The osseous changes are marked on the left and moderate on the right.

Fig. 2-*A*. Photograph of same patient's feet showing the ulceration which was improved by irradiation of the lumbosacral cord.

standing. We feel, therefore, that syringomyelia or some very unusual condition must be considered as the etiologic factor. The patient received a series of roentgen treatments over the lumbar spine. July 29, 1936, the patient was found to be working full time. He felt that the feet were better since the roentgen treatment, and examination showed some healing of the ulcers.

Case 2. H. G. (K 13,184), white, male, single, aged 34 years, was admitted May 3, 1935. He denied venereal disease.

*Family History.*—A great-uncle, two uncles, two cousins, and one second cousin have trouble with their feet.

*Past Medical History.*—"Intestinal flu" in 1929. No injuries.

*Present Illness.*—In 1922 a callus formed on the ball of the right great toe. In 1925, the terminal phalanx of the right great toe was removed for a chronic painless ulcer: post-operative healing was slow. In 1926, another painless ulcer appeared on the stump. The doctor probed back two inches but the patient could not feel it. In 1927, the stump of the right toe was removed. In 1928, the right second toe was removed for "hammer toe" and later re-amputated when the stump grew sore. In 1932, the patient tried to remove a painful callus from the ball of the right toe and there has been an ulcer there since. There has been no trouble with the left foot. The general health is normal. The patient can walk quite well: he has no pain except a strain in the right calf from walking on the heel. General examination is negative. The blood count, Wassermann reaction, spinal fluid, and urine are all normal. Examination of the extremities shows absence of the first and second toes from the right foot and part of the adjacent metatarsus. There is a callus on the ball of the right foot. Pain, thermal sensation, and pallesthesia are lost on the toes of both feet. Knee-jerks, 2+/2+; tendo-achilles, −/−; plantars, −/−.

*Roentgen Examination.*—Anteroposterior and lateral films of the right foot show resection of first and second toes and distal ends of the metatarsals. The end of the third metatarsal is greatly narrowed and shows an old healed fracture: the fourth and fifth appear normal. There is no x-ray evidence of active osteomyelitis or of bony disease in the left foot.

Case 3. H. S., white, female, single, aged 37, was examined June 13, 1936.

*Family History.*—Grandfather, father, three aunts, and four cousins have foot trouble similar to patient.

*Past Medical History.*—Ordinary dis-

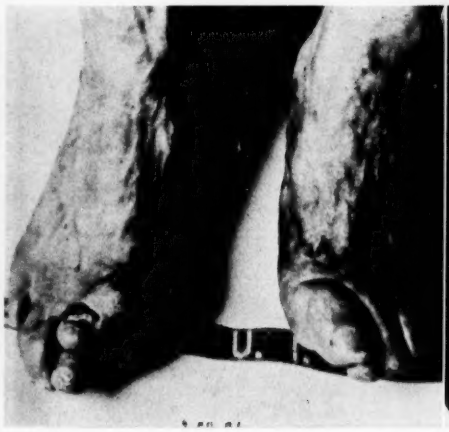

Fig. 2-*B*.

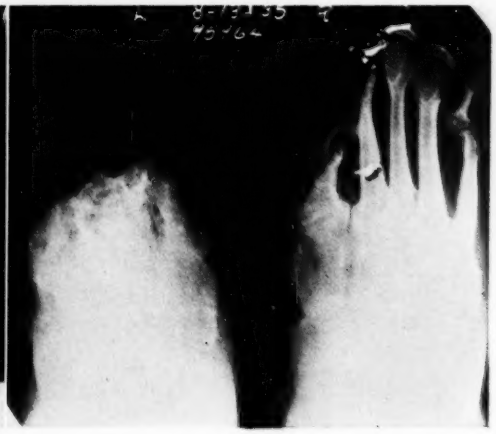

Fig. 3-*A*.

Figs. 2-*B* and 3-*A*. C. J., male, aged 45 years. An elder brother of patient shown in Figure 1, showing marked osseous and soft-tissue change. Ultimately came to amputation of the left foot.

eases of childhood. No injuries. No operations except upon her feet.

*Present Illness.*—This began at the age of 13 years at which time she had painless ulcers, persisting "off and on" ever since, on both feet. They may heal rapidly or slowly. At times, the feet become swollen, and she has had episodes of chills and fever lasting from several days to some weeks.

Until 1932, the right foot was always the worse. For years, there have been discharges of bone particles from each foot. In 1932 the left foot became more swollen than its fellow and in 1934 her doctor opened an abscess on the left foot and removed some dead bone. This was repeated in 1935. There has been no feeling in the toes for ten or more years. At the time of the second operation she felt no pain although the doctor did not use an anesthetic. Except for an occasional day, the patient was able to work until April 21, 1936, although she has had to wear a large shoe on the left foot. She lost one job because of the odor arising from the feet. Her general health, appetite, sleep, bowel and bladder functions have been normal. She has had no trouble with the hands. In fact, she has been normal except for the trouble in the feet.

General examination shows a healthy appearing white woman, 37 years old. Speech and mental state are normal. Weight estimated at 138 pounds and the height at 67 inches. She comes to the door on crutches and does not put the bandaged left foot to the floor. The cranial nerves and arms are normal. The legs are of normal appearance above the ankles except that the left calf is 2 cm. larger than the right. Both feet are deformed and the left is swollen. There is a 2 cm. chronic ulcer on the ball of each foot. The deformity is most marked on the inner side of the feet because of the retraction of each big toe. On the left, the fourth toe extends farthest forward and on the right foot, the second. The feet are not tender. The skin is warm on both feet. The strength is normal in both legs except for 15 per cent flexion and extension in the toes on the left. Knee-jerks, 3+/3+; tendo-achilles, −/−; plantars, −/−. Pallesthesia and light touch are normal on the toes: pain sensation is lost: light touch is intact on the shins.

*Roentgen Examination.*—Dorso-plantar projections of both feet show marked deformities consisting of absorption of the proximal ends of the metatarsals, disintegration of the second and third metatarso-phalangeal joints of the left foot, the tarso-metatarsal joints of the same foot, absorption and attenuation of many of the

Fig. 3-*B*.

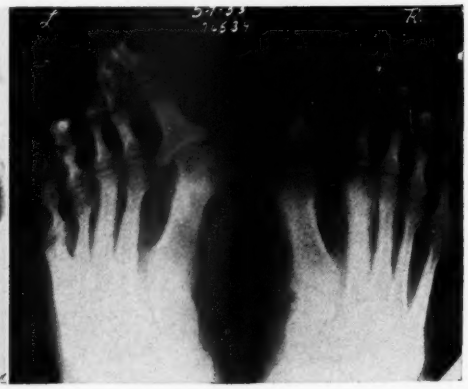

Fig. 4-*A*.

Figs. 3-*B* and 4-*A*. E. T., male, aged 36 years. This patient came to us in 1933 with plantar ulcers and these early bone changes, but we did not fully appreciate their significance. Re-examination after three years showed marked progression of the process, which we now consider as "typical."

metatarsals and phalanges. There is complete loss of some of the terminal phalanges.

*Impression.*—The findings in this case are not dissimilar to those found in several other cases and probably have a neurotrophic basis. Syringomyelia would be our first impression.

Case 4. H. W. (M 1263), white, female, single, aged 70 years, was admitted on Aug. 23, 1935.

*Family History.*—Father died of cancer of the hand: mother died of a stroke: five brothers and sisters alive. One sister has feet like the patient's. Six brothers and sisters are dead (three as children, one at 71, and two at 76).

*Past Medical History.*—No fevers, operations, or injuries.

*Present Illness.*—At the age of six years she had epidemic meningitis and has had trouble with her feet ever since, so that she has never been able to dance, hop, or run. There has been increasing stiffness of the legs. She has used a cane for the last four years and now can walk only with help. At the age of 40, an ulcer appeared on the end of the right great toe which was later amputated. The legs have ached and have been sore all her life but have never been numb. The palms of the hands have been bony and dry all her life. General health, appetite, sleep, bowel and bladder functions have always been normal.

General examination shows 3+ spastic paraplegia; bicep-jerks, 2+/1+; abdominals, −/−; knee-jerks, 2+/2+; tendo-achilles, −/−; plantars extension/extension. Deep sensory impairment below the knees. Pain, light touch, and thermal sensations are intact. There is hyperkeratosis of the skin of the hands and feet, with dystrophic nails.

*Roentgen Examination.*—A single dorso-plantar film of both feet shows complete absence of the first digit and first metatarsal on the right foot, with what appears to be marked ulceration of the soft tissue in this region. The other bones show considerable sclerosis, with some swelling of the distal ends of the toes of the right foot. There is moderate osteoporosis of the bones of the right foot. Those in the left foot are suggestive of trophic changes in the feet, probably on the basis of vascular disturbance.

Films of the hands show moderate osteoporosis of the phalanges with some slight periosteal thickening. Films of the thoracic and lumbar spine show moderate hypertrophic osteo-arthritic changes. Skull films show thickening of the frontal bone such as is not infrequently seen in elderly women.

*Remarks.*—This case differs from those

Fig. 4-*B*.

Fig. 5-*A*

Figs. 4-*B* and 5-*A*. Same patient as shown in Figure 4-*A*. This photograph shows well the deformities and soft-tissue change.

in the "J," "S," and "G" families in that the sensory loss is of the deep rather than of the superficial type, in the larger area of loss, in the smaller amount of ulceration and bony loss, and in the presence of the hyperkeratosis.

The occurrence of a similar condition in a sister and the absence of sphincter disturbance make it unlikely that the condition is a residual of the meningitis which is said to have occurred at the age of six years.

*Laboratory Tests.*—The urine, Wassermann reactions, and spinal fluid are negative. Blood count: red blood corpuscles, 4,000,000; white blood corpuscles, 5,800; 89 per cent hemoglobin.

Case 5. J. H. (M 995), white, male, aged 54 years, divorced; no children; was admitted on Aug. 19, 1935. Denied venereal disease. Patient uses tobacco and alcohol rather to excess.

*Family History.*—No similar condition.

*Past Medical History.*—No fevers or injuries. Cancer removed from scrotum in 1930.

*Present Illness.*—In 1923, while putting up ice, he froze his feet at 15° below zero; did not call doctor; returned to work in four days. From 1923 on, soles were scaly. In 1928 an ulcer formed on the ball of the left foot back of the great toe and later other ulcers appeared and pieces of bone discharged. Toenails came off with considerable pain. His physician began to remove pieces of bone at this time. In 1930 a painful swelling appeared on the inner left ankle, and was opened. In 1933 a sore appeared on the sole of the right foot back of the fifth toe and pieces of bone came out. Later, similar ulcers and bony spicules appeared at the base of the great and fourth toes. There has been little change for the last two years except a discharge of blood "off and on" from the ball of the right foot. The patient can still feel hot and cold, and also pain if he bumps his feet. He can walk any distance. His bowel and bladder functions are normal.

*Positive Signs.*—Deformed feet, principally through shortening; loss of pallesthesia, and pain over the toes; calluses on soles. Knee-jerks, 3+/3+; tendo-achilles, +/+; plantar flexion absent. Pulsations are absent in both dorsalis pedis arteries but normal in posterior tibials. Pupils, 3/3.5 mm.; light reactions 10/10; accommodation reactions, 80/100.

Fig. 5-*B*.

Fig. 6.

Figs. 5-*B* and 6. E. L. S., female, aged 46 years. This patient is of the third generation of the "S" family, in which two preceding generations have had a similar condition.

*Roentgen Examination.*—Dorso-plantar and lateral films of the feet show deformity of the phalanges and metatarsals and loss of part of the phalanges and atrophic changes of the other bones. The proximal phalanx of the third right digit shows what appears to be a pathologic fracture without evidence of sequestra but with periosteal change. There is also periosteal new bone along the distal end of the shaft of the third metatarsal. There is ankylosis of the first metatarsal phalangeal joint of the right foot. The changes noted here may possibly be due to circulatory disturbance, but we believe it is mportant to have the patient examined for changes in the central nervous system, particularly syringomyelia.

*Impression.*—Trophic changes in both feet suggesting central nervous system disease; osteomyelitis of the third proximal phalanx of the right foot.

*Eye Examination.*—Vision, OD 6/60; OS 6/90; primary optic atrophy and retrobulbar neuritis; fields slightly constricted; slight central scotoma.

*Laboratory Tests.*—Blood count: red blood cells, 4,400,000; white blood cells, 9,300; 75 per cent hemoglobin; Wassermann reaction negative. Spinal fluid (lumbar puncture) clear, 11 cells, globulin negative, Wassermann negative. Repeat lumbar puncture shows clear fluid, globulin—slightest possible trace, pressures 10–12–15–20, Wassermann negative.

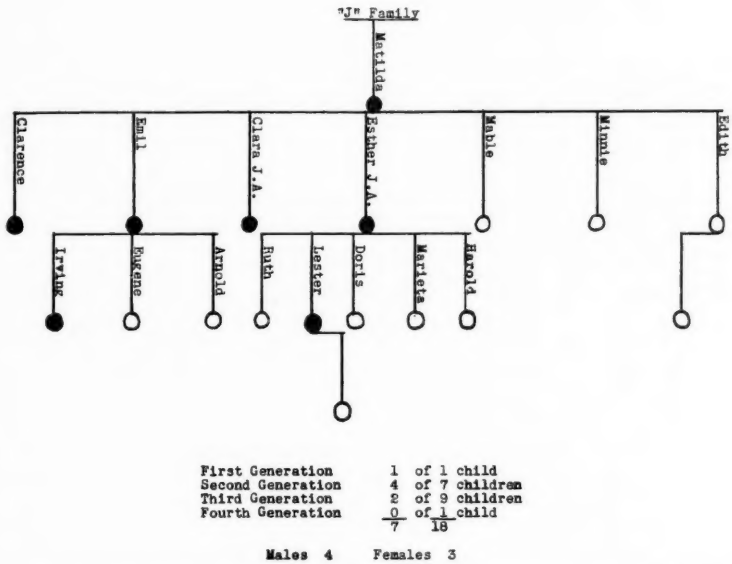


Fig. 7. "J" family tree, showing one case in first generation, four cases in the second, and two in the third.

## ROENTGEN CHARACTERISTICS

Joint changes accompanying lesions of the spinal cord were emphasized by Mitchell (41), in 1831 and again in 1833, and the connection has been recognized since that time. Charcot (10) established the relationship of joint lesions and tabes, and Schultz (57), in 1883, demonstrated that joints similar to these were present in proved cases of syringomyelia. According to Graf (21), the pathologic anatomy of joints affected by syringomyelia is not essentially different from that caused by tabes, and this fact has been stressed by other writers. More recently, Zimmer (68) has called attention to the fact that

these changes may be either hypertrophic or atrophic. Morvan (42), in 1883, described a syndrome in which cervicodorsal syringomyelia produced painless panaris, with muscular and osseous atrophy. This syndrome comes closest to simulating, in the upper extremity, the findings as we have observed them in the lower extremities, although his cases showed no familial tendency.

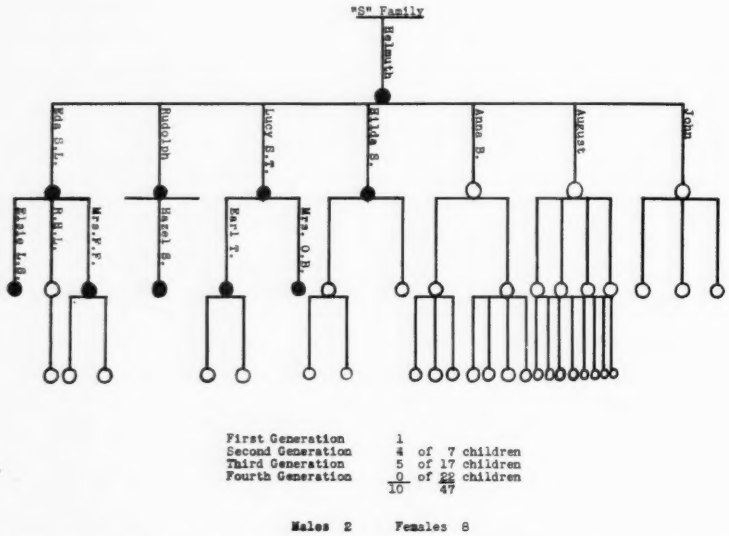


Fig. 8. "S" family, showing one case in first generation, four in the second, and five in the third.

Emphasis on joint changes in syringomyelia has been laid by many writers (Pokorny, 48, Balestra, 3, Esau, 15, Camplani, 9, Halstead and Dick, 27, and others), while Köhler, A. (34), Kofend (33), Köhler, P. (35), Alajouanine, d'Allaines, and Saucier (1), Tedesco (61), and others have laid stress on such changes as subluxations, bone atrophy, and spontaneous fractures, speaking particularly of the shoulder joint and humerus. As has been emphasized by Schlesinger (56) in his monograph on syringomyelia, bone and joint changes in this condition are much more common in the upper extremities, occurring there in 80 per cent of the cases as against 20 per cent in the lowers. Certainly one good reason for this is that syringomyelia occurs much more commonly as the cervicodorsal type. In tabes, the percentage of upper and lower extremity involvement is almost the reverse of that found in syringomyelia. In Graf's series of 51 joints, only once was the foot affected, while of Schlesinger's 148 affected joints, eight only were in the feet. Periosteal new bone formation is not an infrequent occurrence in syringomyelia and appears without relation to soft tissue or secondary bone infection.

Aside from roentgenograms made to determine the presence or absence of spina bifida occulta, our roentgen observations have been confined almost wholly to the feet and ankles. From our radiographic examination of 15 cases, we have come to consider "typical" changes as consisting of attenuation and absorption of the distal portions of the metatarsals with or without similar involvement of the phalanges (Figs. 1-2-*B*). These findings are usually associated with disintegration of the metatarso-phalangeal joints. The first change noted may be only a roughening and sclero-

sis of the shafts of the metatarsals or even an early porosis, usually of the first. Thickening of the periosteum of a metatarsal is not an unusual finding but it is less commonly found on the tibia and fibula. Loss of digits spontaneously or by surgical amputation is common (Figs. 3-*A* and 3-*B*). The great toe and first metatarsal may show the first changes but this is by no means an invariable rule (Figs. 4-*A* and 4-*B*). Fracture of the atrophic end of a metatarsal or of a phalanx is not uncommon, while ankyloses of small joints may occur (Fig. 6). This latter finding may be due to secondary infection of the joint through a perforating ulcer. Schlesinger (56), however, points out that this is more common in the hands than in the feet. Because of the physical activity of these patients, made possible through lack of pain, one almost never sees disuse osteoporosis, and fractures cannot be assumed to be on this basis. This point is also stressed by Clarke and Groves (12). While both feet may be involved equally in the pathologic process, it is not uncommon to have only one foot visibly affected. It is, of course, not infrequent to have early neurologic changes and even soft-tissue change, such as cheiromegaly as mentioned by L'Hermitte and Nemours (37) (Figs. 5-*A* and 5-*B*) and trophic ulcers, without being able to demonstrate bone or joint abnormality.

The above changes are to be differentiated from rather similar ones found in patients who have been repeatedly exposed to cold and damp, so-called "trench foot,"

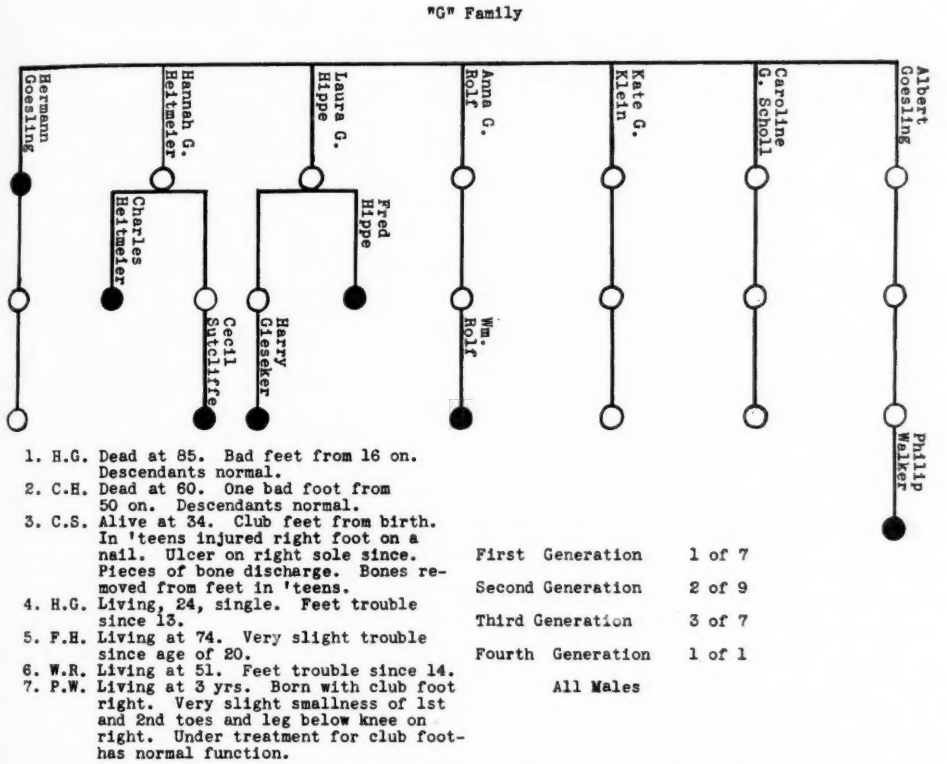
"G" Family
Hermann Goesling
Hannah G. Heitmeier
Charles Heitmeier
Cecil Sutcliffe
Laura G. Hippe
Fred Hippe
Harry Gieseker
Anna G. Rolf
Wm. Rolf
Kate G. Klein
Caroline G. Scholl
Albert Goesling
Philip Walker
1. H.G. Dead at 85. Bad feet from 16 on. Descendants normal.
2. C.H. Dead at 60. One bad foot from 50 on. Descendants normal.
3. C.S. Alive at 34. Club feet from birth. In 'teens injured right foot on a nail. Ulcer on right sole since. Pieces of bone discharge. Bones removed from feet in 'teens.
4. H.G. Living, 24, single. Feet trouble since 13.
5. F.H. Living at 74. Very slight trouble since age of 20.
6. W.R. Living at 51. Feet trouble since 14.
7. P.W. Living at 3 yrs. Born with club foot right. Very slight smallness of 1st and 2nd toes and leg below knee on right. Under treatment for club foot-has normal function.
First Generation 1 of 7
Second Generation 2 of 9
Third Generation 3 of 7
Fourth Generation 1 of 1
All Males

Fig. 9. "G" family, showing one case in first generation, two in the second, three in the third, and possibly one in the fourth.

and in which the changes are probably a direct result of a vascular disturbance. Similar changes have also been reported in the hands and feet of cases of chronic long-standing psoriasis although we have never had such a case of our own.

Trophic changes in the feet, soft tissue, bones, and joints have been reported by various observers but there has been no unanimity of opinion regarding the etiology. Mertens (40), in 1901, presented a detailed discussion of a patient with foot changes similar to those we are presenting and his impression was that the patient had trophic changes due to a lumbosacral syringomyelia, sporadic in nature. On the other hand, Clarke and Groves reported similar changes in a brother and sister and emphasized that the bone and joint changes may be so pronounced that attention may be diverted from syringomyelic symptoms. The presence of a spina bifida occulta as a necessary or common finding in these cases has been emphasized by Thévenard and Coste (63), Kienböck (31), and others, but in our group we have no evidence that it plays a part. The difficulty of differentiating this condition from trophic dactylomegaly due to tabes has been mentioned by Alajouanine, Mage, and Mauric (2), while Neumeister (45) stresses the point that bone and joint changes as well as perforating plantar ulcers may be the first symptoms of syringomyelia, and reports seven such cases. Borchard (6), in a detailed discussion of the bone and joint changes in syringomyelia, points out that nerve changes may cause direct trophic bone changes or may act through the peripheral vasomotor system.

### ROENTGEN THERAPY

The first case of syringomyelia treated by the roentgen ray was reported in 1905 by Raymond, Oberthur, and Delherm (51, 52). The young woman showed sensory and motor improvement for a period of at least three years. By 1912, Sahatchieff (55) was able to collect 30 cases and estimated that approximately 80 per cent were improved. By 1930, 159 treated cases could be collected and still 79 per cent showed improvement. Czerny and Heinismann (13) report 124 cases: of the 70 which had been followed for from two to five years, 75 per cent were benefited. All of their cases had progressed up to the time they received treatment. These authors are certain that the sensitivity of the skin to roentgen rays is not increased in syringomyelia. Delherm (14) emphasizes the fact that the earlier the disease, the better are the results of irradiation, but that no case is too advanced to at least warrant one in attempting the alleviation of symptoms.

TABLE IV

| | "G" Family | "J" Family | "S" Family | "W" Family | Sporadic | Total |
|---|---|---|---|---|---|---|
| Males | 7 | 4 | 3 | 0 | 1 | 15 |
| Females | 0 | 3 | 7 | 2 | 0 | 12 |
| | | | | | | 27 |

He also states that pain is the first symptom which is influenced. This has also been the experience of O'Brien (46), Haworth (28), and others, including ourselves. Parasthesias are next improved, while thermal sensation and motor disturbances respond slowly. Disease of longer duration than from eight to ten years is unlikely to show improvement, while young patients do better than older ones. Giese and Ossinskaja (18) report 128 cases treated, with 50 per cent improved, 30 per cent arrested, and 20 per cent unaffected. They state that bulbar cases do especially well.

The most convincing observations on the pathologic effect of irradiation on syringomyelia have been made by L'Hermitte (38) and his co-workers and later by Heinismann and Savenko (29). In a woman with typical cervicodorsal involvement who had been irradiated and later died of double empyema, L'Hermitte found complete disappearance of all pathologic glial tissue in the parts treated and no change elsewhere. These observers also found no effect on the vascular tissue.

No case similar to ours has had microscopic examination following irradiation, so

that no conclusions can be drawn. Three of our cases have been irradiated and two have shown beneficial effect. We feel, therefore, that this is additional evidence that we are dealing with at least a syringomyelia-like condition and not a purely developmental anomaly such as one encounters in spina bifida or the so-called myelodysplasia.

## SUMMARY

We have examined 19 of the 27 cases included in this report. Twenty-six of these cases occurred in four families, while in the other case, we have been unable as yet to establish a familial tendency. These cases can be tabulated as in Table IV.

Because of the neurologic findings, though not entirely typical of syringomyelia, we feel that we are dealing with an entity which can well be described as "familial lumbosacral syringomyelia." While both the neurologic and roentgenologic findings can be found in tabes, this has been a relatively infrequent finding in our experience, and of course none showed a familial tendency.

Of the 19 examined cases, the feet showed calluses in 16, one or more ulcers in 17, and pain, usually slight, in six. The knee-jerks were normal in 18, tendo-achilles reflex absent in 12, and plantar extension absent in one or both feet in nine. Pallesthesia was impaired or lost in 16, hyperkeratosis was present in the hands of two cases, and in a third case, the skin of the hands was dry and thick.

Roentgen examination of the feet showed osseous changes in 15 cases. These changes were trophic in character—absorption of bone, disintegration of joints, periosteal new bone, and pathologic fractures. Soft-tissue changes could also be seen. Films of the lumbosacral spine convinced us that spina bifida occulta *per se* is not a necessary

TABLE V.—PERTINENT DATA ON ALL OF THE CASES WE ARE REPORTING

| | Sex | Age | Age of Onset | Calluses | Ulcer | Pain | K. J. | T. A. | Pl. | X-ray | Sensation on Toes: Pall. | Pain | Cotton |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| G. Family | | | | | | | | | | | | | |
| W. R. | M | 51 | 18 | 3+ | 3+ | 2+ | +/+ | −/− | −/ex | 4+ | O.K. | O.K. | |
| H. G. | M | 34 | 21 | 1+ | 1+ | 1+ | 2+/2+ | −/− | −/− | 3+ | Lost | Lost | |
| C. H. | M | 60 | 49 | − | 1+ | − | 1+/2+ | 1+/1+ | ?/ex | 3+ | 15% | 75% | |
| C. S. | M | 31 | 14 | − | 4+ | ± | 1+/1+ | −/− | −/− | 4+ | Impaired | Impaired | |
| F. H. | M | 74 | 20 | 1+ | ± | − | +/+ | −/− | −/− | 1+ | Impaired | Impaired | |
| P. W. | M | 3 | Birth | − | − | | −/− | −/− | −/− | | O.K. | ? | |
| H. G. | M | 85 | 16 | 4+ | 4+ | | (Not examined.) | | | | | | |
| S. Family | | | | | | | | | | | | | |
| L. J. | F | 59 | 51 | 3+ | 1+ | ± | 2+/2+ | −/− | −/− | 1+ | O.K. | 20% | |
| H. S. | F | 37 | 13 | 3+ | 4+ | 1+ | 3+/3+ | −/− | fl/? | 4+ | O.K. | Lost | |
| E. T. | M | 36 | 27 | 3+ | 3+ | − | 2+/2+ | 1+/− | −/ex | 3+ | Lost | Lost | |
| Mrs. R. S. | F | 46 | 12 | 2+ | 4+ | ± | 2+/2+ | −/− | −/− | 4+ | O.K. | Lost | |
| H. S. | M | 70 | Bad feet all his life, with ulcers. Died of heart. at 70. | | | | | | | | | | |
| E. L. | F | 58 | Bad feet all her life, with ulcers. Died of ca. vent. at 58. | | | | | | | | | | |
| R. S. | M | 40 | 15 | | 2+ | | (Not examined.) | | | | | | |
| H. S. | F | | | | 1+ | | (Not examined.) | | | | | | |
| Mrs. F. F. | F | | | | 1+ | | (Not examined.) | | | | | | |
| C. B. | F | 38 | (Indefinite history of slight foot trouble: not examined.) | | | | | | | | | | |
| J. Family | | | | | | | | | | | | | |
| E. J. | M | 41 | 19 | 1+ | 4+ | 1+ | 3+/3+ | 1+/1+ | ex/ex | 4+ | 25% | 25% | |
| C. J. | M | 45 | 18 | 1+ | 4+ | 1+ | 3+/3+ | −/− | −/− | 4+ | Lost | 0 | 0 |
| I. J. | M | 17 | 15 | − | − | ± | 3+/3+ | 1+/1+ | ex/ex | 1+ | Lost | Lost | Lost |
| E. A. | F | 43 | 8 | 1+ | ± | − | 3+/3+ | −/− | ex/ex | − | Lost (?) | Lost (?) | Lost (?) |
| C. W. | F | 38 | 13 | 1+ | 1+ | − | 1+/1+ | 1+/1+ | ex/− | − | 60% | 50% | 50% |
| L. A. | M | 16 | | 1+ | 1+ | − | 2+/2+ | 4+/4+ | ex/ex | − | O.K. | 25% | 0 |
| M. J. | F | 69 | 15 | (Dead. Never examined. Legs 1+ stiff and gait of short step type. Had legs amputated for diabetic gangrene some years before death.) | | | | | | | | | |
| W. Family | | | | | | | | | | | | | |
| S. W. | F | 65 | 4 | 3+ | 3+ | ± | 2+/2+ | 1+/− | ex/ex | 3+ | Lost | O.K. | |
| H. W. | F | 70 | 6 | 1+ | 2+ | − | 2+/2+ | −/− | ex/ex | 3+ | Lost | O.K | |
| Sporadic case | | | | | | | | | | | | | |
| J. H. | M | 54 | 46 | 1+ | 2+ | 1+ | 3+/3+ | 1+/1+ | fl/fl | 4+ | Lost | Lost | |

part of the syndrome. Of six cases, two showed a small cleft.

In four cases, there were episodes of severe infection. One case of chronic infection necessitated amputation below the knee. In only one patient, P. W. of the "G" family, has there been a possible appearance of the condition in the fourth generation. One family showed an associated case of striate diplegia with athetosis. The sporadic case showed unequal partial Argyll Robertson pupils, primary optic atrophy, and retrobulbar neuritis with slightly constricted fields. His vision was OD 6/60 and OS 6/90. We agree that this case may be one of tabes but we have included it because we have not seen similar changes in the feet occurring in tabes and because these changes are typical of those in the familial groups.

The fact that at least two of these cases have shown progression over a period of years and two others have been benefited by roentgen irradiation to the lumbosacral spine makes us feel that we are dealing essentially with a condition closely akin to syringomyelia. We have, therefore, chosen to designate this condition as "familial lumbosacral syringomyelia."

## CONCLUSIONS

1. The occurrence of chronic painless ulcers on the feet, especially when associated with roentgen evidence of neurotrophic changes in the bones and joints of the forefeet, should lead to a study of the family history in a search for similar cases.

2. Familial lumbosacral syringomyelia is one of the most frequent causes for such a syndrome.

3. Irradiation of the lumbosacral cord appears to be the best available treatment.

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# THE NEW ALCHEMY[1]

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WITH ADDED REMARKS BY R. R. NEWELL, M.D., SAN FRANCISCO

THE title assigned me was "The Romance of the New Alchemy." I asked to have the first three words dropped, but it is only fair that we share what may seem like romance in physics with you in medicine, who are working on the borderlines of equally romantic fields. In casting about for something to take along with me from Washington, I thought it would be best to bring you the real thing. So, before the end of this talk, we shall actually show you some atoms which have been perfectly good-natured, stable atoms since the earth was born out of the sun, excite them to radio-activity, and observe their transmutation into atoms of another chemical element. This is the new alchemy.

First, let us orient ourselves with respect to the six-foot world in which we live. Figure 1 shows the scale of sizes from the smallest to the largest. Man stands not quite at the middle of the scale, but the smallest things are, to him, just about as extreme as the largest ones. The subject of this paper deals with something very tiny indeed, the atomic nucleus, shown at the upper left in the figure.

Most of you are familiar with chemical reactions: sodium hydroxide combines with hydrochloric acid to form salt and water—things of that kind. Chemical reactions, and the forces between the atoms in a molecule, are electrical—electrical in a special sense—but, nevertheless, electrical forces.

However, as we go down inside the atomic nucleus, we come to a new region which was first investigated at the end of the last century by the discovery of radio-activity. It was found then, in the course of ten or twelve years, that atoms were exploding and changing from one kind of chemical atom into another. Thus investigators became aware of the instability of certain atoms. True, these were the heaviest atoms at the heavy end of the atomic table, but atoms were no longer the immutable elements they had been thought for a good many years to be.

To explain these and other facts, Rutherford proposed the model of the atom which bears his name. Chemical forces are concerned with the electrons on the outside of the atom, the simplest of which is a hydrogen atom with a simple nucleus and one electron. Complicated atoms become more and more picturesque. Chemistry deals with the interaction of the forces on the outside, whereas in nuclear physics we are concerned with the small speck at the center, about one ten-thousandth of the total diameter of the atom, but containing practically the entire mass.

Perhaps the most important thing about the Rutherford nucleus was the determination of the ratio of the size of this nucleus to the size of the atom. On shooting atomic particles, helium nuclei (from the radioactive elements), at atoms of the ordinary elements, they were found to be practically transparent. The rarity of direct hits, nucleus against nucleus, afforded a measure of the smallness of the nuclear diameter. That was in 1911. Another thing was presently discovered, namely, the existence of isotopes—that elements may have apparently identical chemical properties and still be different in actual mass or weight.

In the course of the next five years, culminating in one of Rutherford's experiments in 1919, it was shown that hydrogen could be knocked out of nitrogen by these fast alpha particles. This was the first ob-

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Ga., Dec. 11–15, 1939.

served reaction in artificial nuclear physics. It is true that Rutherford used a natural source of fast alpha particles (radium or

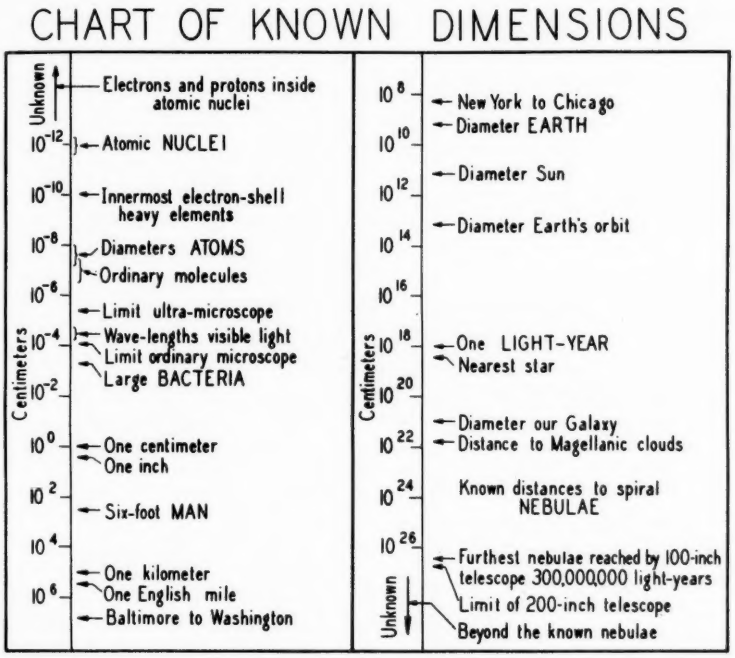



Fig. 1. The nucleus of an atom is the smallest region of space about which we have ideas or conceptions. It is approximately as far removed from the sizes of familiar things as are the furthest spiral nebulæ visible in the 100-inch telescope at Mount Wilson.

lar to the hydrogen nucleus but without any charge and, hence, without any accompanying electron.

mesothorium), but he produced and demonstrated transmutations at will. During the following five or six years, until 1925, similar transmutations were demonstrated in a number of the lighter elements: knocking hydrogen particles out of boron, nitrogen, aluminum, silicon, etc. Phosphorus was, I think, the heaviest one. These reactions indicated a new chemistry of the atomic nucleus. It was clear that the nucleus was made up of a good many parts which had a way of combining somewhat similar to the combinations of atoms in ordinary chemistry.

This great story of the first exploration of a new region of space, intimately close to us yet incredibly far removed, culminated with Chadwick's discovery, in 1932, of the neutron, a heavy particle quite simi-

So, the atom is not indivisible, but, in fact, consists of many parts. This brings us to the present list of elementary particles. There are two heavy particles: the proton, which is the core of the hydrogen atom, and the neutron, very similar to it—the same mass but without any electrical charge (Fig. 2). Then there is a series of electrons. The negative electron is the ordinary one in the outside shell of the atom; the positive electron is transient, it combines with the negative and disappears in radiation; heavy electrons (or "mesons") are transient states of existence of electrons at very high energies. There are some hypothetical particles called "neutrinos" which may or may not exist. This is really just a name for some of our difficulties in physics.

I cannot leave the list of particles with-

out mentioning the photon. The light wave, in some of its reactions, behaves much like a particle and perhaps should be included, as the photon, in the list of elementary particles.

forces, proton-neutron forces, and neutron-neutron forces. One of the most interesting and, undoubtedly, fundamental facts that has been uncovered in the last three or four years is this: these three forces are all

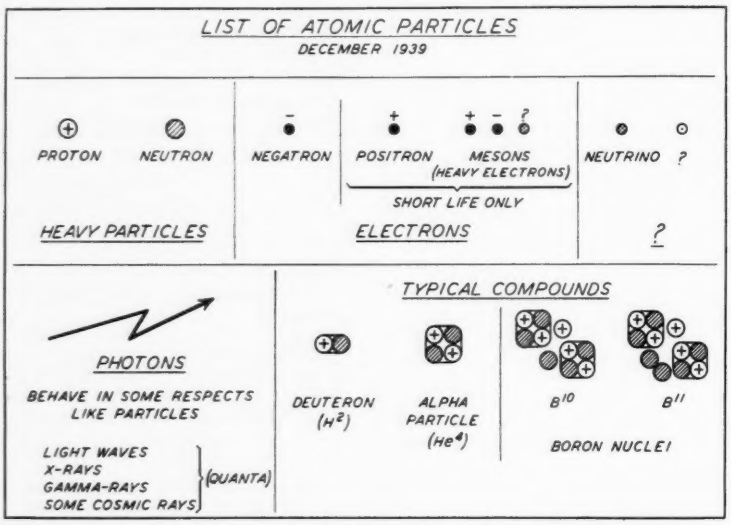



Fig. 2. All material things are believed to be built up from a few "fundamental particles." Atomic nuclei are now thought of as constructed from protons and neutrons, as indicated here.

The atomic nuclei are built of two kinds of heavy particles. The simplest combination is the nucleus of heavy hydrogen, the deuteron, which is composed of one proton and one neutron (see Fig. 2). The alpha particle or helium nucleus is built of two protons and two neutrons. The forces that hold these particles together have attracted considerable interest, and it develops that these are short-range forces. They effectively extend only a millionth of a millionth of an inch away from the particles themselves. In other words, a proton or a neutron must get that close, a millionth of a millionth of an inch, before it experiences any of the attractions that bind the particles together, in contrast to chemical forces, roughly a hundred thousand times longer in range.

Since there are two particles—protons and neutrons—there is an opportunity for three interaction forces: proton-proton alike. They are practically equal in magnitude and behave quite similarly. All are extremely short-range forces.

This is the basis on which nuclei are built, and these short-range nuclear forces are fundamental in the same sense that gravitation and electromagnetic forces are fundamental. These three kinds of fundamental forces cannot be classified as derived from some other type of force, while, for example, forces of impact, cohesion, elasticity, etc., are basically electromagnetic in nature.

The mass of a nucleus is the number of protons and neutrons it contains. The chemical nature of it depends on its charge, that is, on the number of protons (only). Isotopes have the same charge but different weights: many stable isotopes are found in nature. Hydrogen, for example, exists in three forms: a proton with no neutron, with one neutron, and with two neutrons.

The heavier elements never have pure proton cores. There are always many neutrons, too, so that the weight increases faster than the nuclear charge.

In addition, we find at the heavy end of the table the unstable elements, the natural radio-active elements, which first introduced us to the idea of instability inside the nucleus.

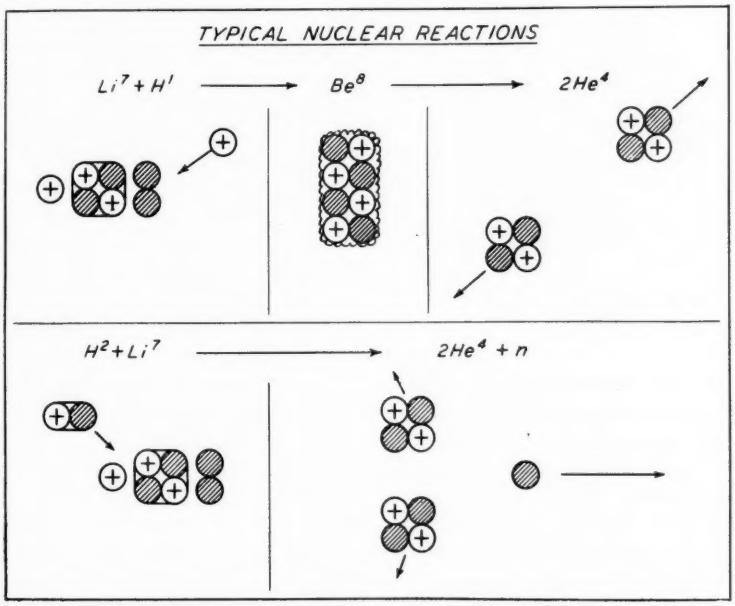



Fig. 3. The first nuclear transmutation produced by artificial means (using a high voltage beam) was the transmutation of lithium into helium by bombardment with ordinary hydrogen nuclei. When nuclei of heavy hydrogen are used high speed neutrons are emitted by the lithium target.

For typical nuclear chemistry we might consider what was done in 1932, by Cockroft and Walton (Fig. 3). This was the first completely artificial nuclear reaction to be achieved. Protons accelerated by a moderately high voltage (in a vacuum tube) were made to bombard a lithium target and produced an unstable nuclear compound which broke up into two alpha particles. This picture shows protons bombarding the lithium-7 combination. It forms an unstable compound which is wiggling; it is excited, has too much energy, and flies apart in the form of two alpha particles. That is typical of many of the particle reactions of nuclear chemistry. What we detect are these particles that are flying away; in other words, we detect the immediate radio-activity. The half life of this particular process, like many of these intermediate compounds, is only about $10^{-21}$ second.

Figure 3 also shows a similar example of bombarding lithium-7 by deuterons. Here we get two alpha particles and a neutron. This time the unstable compound broke into three particles, which is typical of many reactions.

I should mention here that in these reactions we see demonstrated in the laboratory the equivalence of mass and energy in accordance with the Einstein theory. If mass disappears, energy will appear in its place. When these reactions occur, we find that the resulting atomic compounds weigh more or less. In general, they weigh less than the original, and the difference has

appeared in the form of the energy of the particles as they fly apart.

Artificial radio-activity, in which atoms of the ordinary chemical elements emit electrons or beta rays just as do the familiar

| ARTIFICIAL RADIO-ACTIVITY<br>Typical Reactions |
|---|
| $\begin{cases} B^{10} + H^2 \longrightarrow C^{11} + n \\ \text{then } C^{11} \longrightarrow B^{11} + \overset{+}{e} \end{cases}$<br>Half life = 20.3 minutes |
| $\begin{cases} Ag^{109} + n \longrightarrow Ag^{110} \\ \text{then } Ag^{110} \longrightarrow Cd^{110} + \overset{-}{e} \end{cases}$<br>Half life = 22 seconds |

Table I. Illustrating two examples of nuclear chemistry.

elements of the radium family, is an aspect of the new alchemy which is of the greatest direct interest in medicine, biology, and chemistry. By introducing a relatively small proportion of these radio-active atoms, produced by high voltage bombardment, into a chemical sample containing the ordinary stable atoms of the same element, one can use the radio-activity, which is very readily detected, as a tracer for this particular sample. This is still true even when the labelled sample is mixed with a large amount of the same chemical element, for example, in the body of an animal. Nuclear processes of the general type shown in Figure 3 often result in combinations which have too few neutrons or too few protons for permanent stability of the combination. Nature adjusts this by having such a nucleus emit a positive or negative electron, thus attaining stability as an atom of an adjacent element (see Table I). This emission process is governed by probability laws, and the unstable tracer atoms have half lives which range from a fraction of a second to many years. ("Half life" is the time required for half of a given sample to undergo the transformation; the total life hence is indefinitely long.) The long-lived species are difficult to produce in useful quantities, however.

Artificial radio-activity has been produced throughout the chemical table, but relatively few of these unstable isotopes have characteristics (half life, production-yield, ease of detection) which make them of great usefulness. Table II lists most of those which appear of immediate interest and value in medical studies.

I might discuss briefly some experiments which are more or less the latest thing in the field of nuclear physics. A new process was made known in January, 1939, called uranium "fission." It may ultimately prove to be a possible source of atomic power. The examples of nuclear chemistry known previously are, in general, like chipping a small piece off a large boulder, when you get to the heavier nuclei. In the example which was discovered last year, the fission of uranium, the large complicated nucleus composed of something like 239 particles (protons and neutrons) divides into two approximately equal units, leaving, for example, barium and krypton.

The most important thing it has given rise to—the most interesting thing from the standpoint of romance—has been the question of whether or not it makes possible the old idea of atomic power. That came about in this way: uranium fission, splitting of the uranium nucleus, is produced by the absorption of a very slow, low-energy neutron. On the other hand, when a uranium nucleus divides into two parts this way, because uranium has a much larger excess of neutrons than do the atoms of about half its weight, several neutrons are freed in each fission, and an energy of nearly 200,000,000 electron-volts is released.

Now, if those neutrons which are released can again be eaten by the uranium atoms nearby, it might lead to a chain process. This is the first time that it has appeared within the realm of possibility to produce atomic power. Numerous experiments on uranium fission have led, to date, only to the result that we cannot say absolutely whether atomic power is or is not possible. However, it is one of those things that the farther you chase it, the harder it seems to be to catch.

The important thing is that although two or three neutrons are emitted from each fission, there are more ways of eating neutrons than by the production of fission, particularly a process of a 25-volt resonance of emitting negatrons (ordinary negative electrons) to form cadmium. The half life is 22 seconds.

Perhaps the most interesting thing to do would be to show the actual production of

SOME RADIO-ACTIVE TRACERS

| Chemical Element | Half Life | Intensity from Cyclotron | Remarks |
|---|---|---|---|
| $C^{11}$ | 20.3 Minutes | $10^9$ $\beta$-rays/sec. | Short half life limits use |
| $N^{13}$ | 10.5 Minutes | $10^8$ | Short half life limits use |
| $Na^{24}$ | 14.8 Hours | $10^9$ to $10^{10}$ | Strong gammas, hard betas; easily measured |
| $S^{35}$ | 80 Days | $10^4$ to $10^5$ | Very soft betas, difficult to measure accurately |
| $P^{32}$ | 14.5 Days | $10^8$ to $10^9$ | Hard betas, most convenient tracer |
| $K^{42}$ | 12.2 Hours | $10^8$ | Radio-sodium usually present |
| $Ca^{41}$ | 250 Days | Weak | Recent discovery; hard to detect |
| $Fe^{59}$ | 47 Days | $5 \times 10^4$ (or less) | Weak; made from rare isotope; soft betas |
| $Br^{82}$ | 34 Hours | $10^8$ | Strong gamma-rays |
| $I^{131}$ | 8 Days | $10^6$ to $10^7$ | Gamma-rays |

Table II. A list of some of the artificially radio-active isotopes of special interest in biology and medicine.

in uranium atoms which eats neutrons quite effectively. Unless special precautions are taken, the neutrons needed to start a chain process are consumed, for example, by this resonance process, which does not lead to fission but to the formation of element 239. The answer is, do not worry about atomic power for the time being. It cannot be excluded absolutely, but it seems to be something that must be followed quite a long way before anything like a real answer is obtained.

Let us return to artificial radio-activity. For example, we bombard fluorine by deuterons to form carbon 11. Carbon 11 is too light to be stable. It gives off a positron (positive electron) and forms boron 11. The average half life for this process is about twenty minutes. This affords a tool for the study of photosynthesis. These short-lived carbon atoms can be traced (detected) by their radio-activity (positrons), and we have been using this radio-active carbon for studies of the carbon dioxide reservoir in plants.

A similar process is the capture of a neutron, similar except that we do not use a high voltage process directly. We use the capture of a neutron by silver to form heavy silver. The heavy silver is too heavy to be stable, and it has a certain probability a radio-active element. In this case I will show the transmutation of rhodium into palladium. [At this point Dr. Tuve began his demonstration.]

We have in the laboratory several types of instruments for detecting radio-activity, one of which detects the electrons that are shot out from radio-active particles. This is such an instrument, called a Geiger-Müller counter. When a fast electron enters the counter, one click or count is heard in the loud-speaker of this amplifier.

To make sure the instrument is working, we have here a small tube, a glow button used for locating the pull-chain on a lighting fixture in the dark. This button was purchased at a ten cent store, and it has about a third of a cent's worth of radium in it. Speaking of romance, radium costs something like a million dollars an ounce, but here, for a nickel, you can get enough radium to give you a great many counts per minute [demonstrates counts]. Every count arises from the explosion of a radium atom, but one ounce of radium contains about $10^{23}$ atoms.

We are sure now that this counter is working because it makes a great many clicks per second. Out in the hall we have a small neutron source (radon mixed with beryllium) that Dr. Henshaw is going to

bring to the platform to activate the rhodium. You will be able to hear the radon coming [the neutron source is brought to the platform and the counter clicks faster and faster]. I have in my hand a sheet of rhodium which I am going to put next to the neutron source, leaving the source still immersed in this tank of water. Water is full of hydrogen, and hydrogen atoms are best for slowing down neutrons. The neutron weighs about the same as a hydrogen atom, so at each collision a fast neutron loses nearly half its energy, on the average.

Did I show that this rodium sheet was not active? Never mind, it will die in a minute, and we will show that it will not be active afterward. [Dr. Tuve had forgotten to hold the sheet of rhodium near the counter to show no initial activity. He now inserted the rhodium into the water near the neutron source.]

The slow neutrons are now being absorbed by the rhodium, which becomes radio-active. The half life is 44 seconds, so I shall leave it there for approximately that length of time and then show that it has become radio-active. Radio-active rhodium, with one neutron too many for stability, decays to form palladium.

This experiment serves to introduce you to the use of artificial radio-active atoms as tracers, on which the following speakers in this symposium will give you a good amount of drilling. I am going to steal a little thunder and tell a hitherto unpublished account of the first time radio-active elements were used as tracers.

I know a friend of Dr. Hevesy, of Copenhagen, who was in Rutherford's laboratory about 1912. Hevesy was a bachelor, and he became tired of the meals at his boarding house—a little suspicious, in fact. One Sunday, he took a little radio-active lead along with him to the table, and left just a small amount on his plate with his meat, after he was through. Thereafter, each day, Monday, Tuesday, Wednesday, Thursday, Friday, he took a sample of the meat to the laboratory and in each sample he was able to demonstrate the existence of a trace of radio-active lead! That was the first case in which radio-active elements were used. [Having passed the required three-quarters of a minute, Dr. Tuve turned again to his experiment.]

This should be amply activated, if you will return the radon source to the hall now. [Dr. Henshaw removed the radium from the platform.] The radon gives such a background of clicks in the counter that it would not be possible to demonstrate the rhodium.

For each click that you now hear, one rhodium atom is exploding and changing into a palladium atom. It shoots out a negative electron and becomes palladium. The rhodium captured neutrons, thereby becoming too heavy, hence unstable.

It is already less active. The half life is 44 seconds; so, in a short time, if I may have another minute, this sample will be practically dead.

CHAIRMAN NEWELL: Will you explain again exactly how you energized that little sheet?

DR. TUVE: Yes. Through the courtesy of Dr. Burnam and Dr. West, of the Kelly Hospital, in Baltimore, I have 50 millicuries of radon mixed with beryllium powder in the lead shield which Dr. Henshaw put into the water. Neutrons are emitted when beryllium is bombarded by alpha particles. That was the neutron source which Dr. Henshaw brought in. I slowed down the neutrons by putting them in the water tank. That is a good means of slowing down because the hydrogen in the water has the same mass as the neutron. A bee-bee shot against a cannon ball bounces, but bouncing bee-bee against bee-bee, on the average half the energy is lost for each collision. It happens that rhodium most easily captures slow neutrons.

CHAIRMAN NEWELL: You mean, if they go too fast, the rhodium could not catch them?

DR. TUVE: That is correct. I want to see if this is dead. [Testing sample.] The counts are much slower, but there is

still a small background, coming, in fact, from some radio-sodium here in my pocket. [Demonstrates activity of radio-sodium.] Well, we have changed a few of the rhodium atoms we held in our hands a few minutes ago, which were rhodium from the beginning of the earth until to-day, into palladium. We have thus contaminated this sample of rhodium to an extremely small degree with palladium.

I want to point out that in addition to using radio-active elements for tracers one may use also the stable elements, stable isotopes. For instance, deuterium has been greatly used for the following of metabolism effects, because one can detect small quantities of heavy hydrogen. Heavy carbon and heavy nitrogen have been similarly used. Other stable isotopes offer further possibilities in the future for tracer experiments.

The methods of detection of the radio-active tracers are, in general, electrical, and you can detect single atoms as they explode. That, however, does not give you complete magic. I must call attention to the general problem of dilution. If you are going to have in the final blood sample only one-millionth of the radio-arsenic that you feed to your rabbit, do not expect to get a large number of counts? If in your original sample you count a million times a second, then you will count only once per second in your final sample—which will not seem very large.

One other problem is dosage. There are limits to the amount of radio-active material that can be fed to any animal without noticeable physiological effects. In general, the dose corresponds to about a third of a millicurie of radio-sodium for a rat, and half that for a mouse (one millicurie is $4 \times 10^7$ beta rays per second). Radio-sodium has a half life of 14 hours, and a dosage of 0.2 millicurie of this element, uniformly distributed throughout a man, gives him a bombardment equivalent to 0.1 roentgen of very penetrating x-rays during 24 hours. With radio-phosphorus, having a half life of 14.5 days, the equivalent allowable dosage is only 0.008 millicurie (8 microcuries), again assuming uniform distribution throughout the body.

I must not forget to point out the fact that when the radio-active activations occur, even when using slow neutrons, there is a large recoil kick (at least a gamma ray is emitted, and this too gives a large recoil). Therefore, you cannot directly activate arsphenamine or any complicated organic compounds. You cannot activate such a compound in its own form, but must synthesize it from the radio-actively labelled element. For example, when we captured the neutron in the rhodium, if the rhodium had been in a chemical compound it would have been kicked out of it by the gamma ray which was emitted without delay. The recoil is perhaps a hundred electron-volts in this case, whereas the forces corresponding to chemical combinations are, at most, three or four electron-volts. So this is a limitation. Tracers, in general, must be synthesized to order from an activated element. You cannot do the synthesis first and the activating afterward.

I did contemplate a demonstration in which I was to eat a little radio-sodium; it has been done frequently. The only trouble is that we have a five-million volt equipment and we are in the midst of building a 16-million volt cyclotron, so we will be exposed to radiation for many years. It is all right for a rat or for a patient, but perhaps not for us.

Note the reaction of our counter through a number of thicknesses of note paper [Dr. Tuve holds envelope over counter]. This envelope contains radio-sodium, about ten-millionths of one curie. Each of those individual clicks is one electron corresponding to the change of one sodium atom to form a magnesium atom. I did not burn my fingers in spite of the fact that it looks dangerous because the strength of the sample is only a few millionths of a curie. However, we probably should not drink this much every time we give a public speech. If I drank the ten microcuries of radio-sodium which I have in this package, it would correspond to nearly one day's tolerance dosage by our standards.

We have adopted as a safe limit in cyclotron work a daily dose not exceeding one-hundredth of a roentgen equivalent. This is one-tenth of the dosage allowed in hospitals. We are exposed to several different kinds of radiation, and neutron exposure may be more dangerous than x-ray exposure. We do not exceed 0.01 "roentgen" of neutron dosage daily, as measured by a Victoreen thimble chamber.

Here is radio-phosphorus also [holds another envelope over counter]. Instead of drinking this I intended putting it in the roots of a plant. However, all the plants in Washington were dormant; it would take two hours to get the activity up the stem, so I just brought along the packages.

This brings up the last point I wanted to make in introducing this symposium, namely, the question of selective effects of radiation. I spoke of the fact that we have several different kinds of new radiation. They all produce tracks of ionization, or produce high speed particles which do so. The main way these radiations differ is in the density of ion pairs along the tracks. A fast electron gives you roughly fifty ion pairs for every centimeter it travels in air; a fast proton gives, maybe, 2,000, and a fast alpha particle from 5,000 to 10,000. This is the main way in which radiations differ; that is, the concentration of the ion pairs along the path of these particles is different. This fact is a long way removed from any specific biologic action. What we do is to produce ion pairs and, perhaps, the fiftieth resultant process in a long chain beyond that point is a specific biochemical action that affects the physiology of a mouse, or some other biologic objective of our use of radiation.

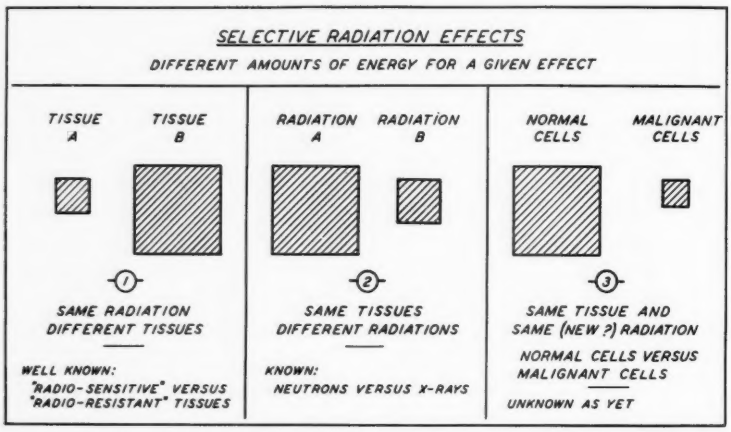



Fig. 4. It is not to be forgotten that radiation therapy is primarily a destructive process. Unless a selective effect of the third type (above) is discovered in the future, primary reliance evidently must be placed on a selective technic rather than a truly selective radiation effect.

In looking for selective radiation effects, just to clarify matters, there are three possible types (see Fig. 4): (1) The same radiation may act differently on different tissues—we are all familiar with this effect; (2) with the same tissues and a different radiation we are less familiar, but neutrons appear to be more effective in some tissues —and incidentally less effective in other tissues—than x-rays. The third—and so far unknown—type, which would be of great aid in the cancer problem, would be a selec-

tive effect between normal and cancerous cells using the same tissues and the same radiation. The thing we would like to find would be a radiation which would greatly damage malignant cells without excess harm to normal cells. Since we still appear to have no real criterion for cancer except the growth of a tumor, the only basis for this search appears to be trial and error.

I wish to clarify this question of the selective effects of radiations by pointing out these three types. Two are known but the third and most desirable effect, if it is possible, at least has not yet been found.

# THE USE OF ARTIFICIALLY PRODUCED RADIO-ACTIVE ELEMENTS AS TAGGED ATOMS IN BIOLOGICAL RESEARCH[1]

*By* WILLIAM FREER BALE, PH.D., *Rochester, New York*

From the Department of Radiology of the University of Rochester, School of Medicine and Dentistry, and the Strong Memorial Hospital

ONE might expect that the carrying out of medical and biologic research involving the radio-active elements would be quite different in method and in the apparatus from that employed for biologic and clinical research. Unfortunately for those of us who are using the radio-isotopes in biologic work, this has not been so. Work carried out with experimental animals still involves metabolism cages, dissections, extractions, and all of the apparatus (mostly beakers, volumetrics and so forth) of the biochemical research laboratory. Also, clinical work still involves collecting and homogenizing urine and feces, taking occasional blood samples, working up operative and occasional autopsy material, and the various clinical chemistry procedures so well known to everyone.

The only impressive or unique apparatus we use at Rochester is the Geiger-Muller counter, the use of which is, of course, by no means limited to measurements of radio-activity. Perhaps most of us know it instead as a sensitive means of detecting lost radium, or as a means for measuring weak x-radiation when r meters and other ionization chambers are not sensitive enough.

Figure 1 shows the type of Geiger-Muller apparatus we are using at the present time (1). In most instances, radio-activity measurements are made on substances in solution. We have persuaded ourselves that this technic most easily leads to quantitative results. Two c.c. of the solution on which activity measurements are to be made are placed in a glass cup which has an inside diameter about two millimeters larger than the radio-sensitive plunger-shaped end of the Geiger counting tube. When the cup is brought up around the tube with a rack and pinion, the solution forms a 1-mm.-thick liquid film surrounding the counting tube. This thin film of liquid, together with the thin counter wall (about 0.003 of an inch thick), only slightly absorbs the beta rays of most of the radio-active elements. Most of the beta rays that are headed in the right direction penetrate into the inside of the counter tube where they give rise to electrical impulses that are amplified and eventually recorded on a mechanical impulse counter. After subtracting a constant background due largely to cosmic rays, the number of counts per minute is proportional to the radio-activity of the solution contained in the cup. Figure 2 shows better the actual construction of the Geiger-Muller tube and the method of mounting that is used.

Radio-iron ejects very soft beta rays. For this element the sensitivity of the apparatus can be increased about five times by electroplating the iron onto the inside surface of a tin foil cylinder that will just slip over the counting cylinder. This procedure eliminates the adsorption of the beta rays by the solution in which the iron is dissolved. The beta rays of radio-sulphur are so soft and non-penetrating that this type of apparatus is not suitable for their measurement. It should be pointed out that there are in use and described in the literature various other types of Geiger-Muller counter set-ups, electroscopes, and electrometers suitable for the measurement of the magnitude of radio-activity in biologic samples.

Rather than deal abstractly with the use of artificially radio-active elements in biologic research it is perhaps of interest to describe some studies of iron metabolism in

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

which the radio-isotope of iron was used as a tool (2, 3). At Rochester, those most intimately associated with this work have been Paul Hahn and George Whipple. The radio-iron was produced in the Radiation Laboratory of the University of California, Ernest Lawrence and M. D. Kamen being collaborators in this work. Radio-active iron is made by bombarding iron in the cyclotron with deuterons. The isotope activated is the one with an atomic weight of 58, the reaction being:

$$Fe^{58} + H^2 \longrightarrow Fe^{59} + p.$$

Since this isotope comprised less than 1 per cent of the total weight of iron, the activities obtained are necessarily rather weak. A typical sample of iron received from California contained 32 mg. of iron in the form of ferric chloride. This iron was dissolved and made up to a volume of 500 c.c. in a volumetric flask. When the activity of a 2-c.c. aliquot was measured with the Geiger counter, it was found to give 120 counts per minute. This represents an activity of 30,000 counts per minute for the entire sample.

The first experiments consisted of feeding aliquots of this radio-iron to (1) anemic dogs (that is, dogs that had been deprived of their iron stores by bleeding while on a low iron diet), and (2) to plethoric dogs (dogs maintained on a diet rich in iron and with their normal body iron supplemented by hemoglobin and colloidal iron injections). These first experiments consisted essentially of taking blood samples at various times following the iron feeding, separating the cells and plasma, chemically extracting the iron from the tissue, and, finally, measuring the radio-activity of this iron in units again of counts per minute on the Geiger counter.

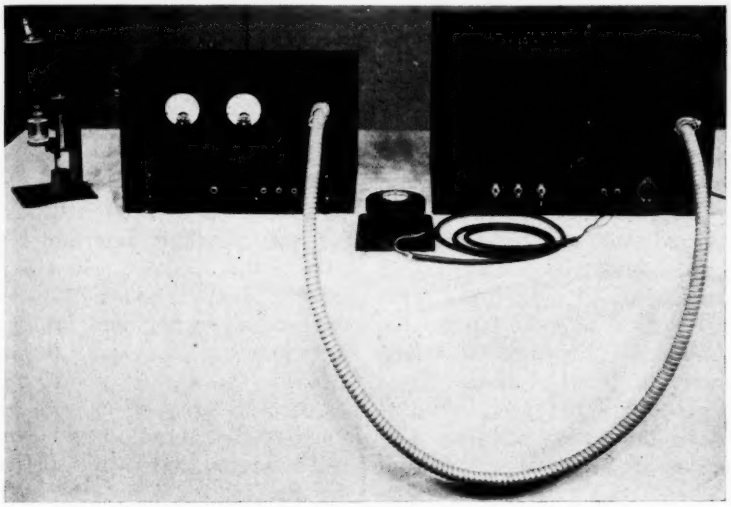


Fig. 1. Geiger-Muller counter.

From hematocrits and blood volume studies done periodically on these dogs it is possible to estimate the amount of the tagged or radio-active iron present in the circulation following feeding.

Before showing typical data obtained, it is perhaps wise to point out that when an atom of radio-iron emits a beta ray such as is detected by the Geiger counter, the nucleus thereby gains a positive charge and becomes an atom of cobalt, the reaction being:

$$Fe^{59} \longrightarrow Co^{59} + e^-.$$

However, up to this instant and during its stay in the dog, it is iron, chemically

inseparable from the ordinary iron present there. True, during its stay in the animal, other atoms of radio-iron, but not this one, had been giving off beta rays and changing to cobalt. But the portion that they made up of the iron in the body was negligible, less than one-billionth of 1 per cent, and the ionization that they produce is a small fraction of an r-unit per day, less than that produced by the beta rays emitted by the normally occurring potassium in the body.

To return to our data, Figure 3 shows the amount of tagged radio-iron present in the plasma and red blood cells of Dog 37-202 following the feeding of radio-iron. This result is quite typical of some ten anemic dogs fed radio-iron. The iron is at first largely transported by the plasma, as is shown by the rapid rise in tagged iron concentration here, but one notes that in a few hours it has almost disappeared from the plasma again.

In the meantime, the tagged iron has started to concentrate in the red blood cells and it will be noted that at the end of three days some 7 per cent of the tagged iron is present in the red cells, presumably as hemoglobin.

The first section of Table I shows the results of several experiments in which radio-iron was fed to anemic dogs. It will be noted that all of these dogs have absorbed appreciable portions of the dose fed, the relative amounts in general being greater as the total amount fed in milligrams decreases. The second section of Table I shows the results of an entirely comparable set of experiments with the exception that the dogs were plethoric—had ample stores of iron already in the body. One notes that these plethoric dogs have absorbed almost negligible amounts of iron.

The conclusion to which one seems led by these data is that the need of the body for iron somehow determines the absorption of this element. In the normal dog in which there is no need for the element, it is absorbed in negligible amounts; in the anemic animal, it is quite promptly assimilated.

Another series of experiments in which the excretion of radio-iron has been studied (4) indicates that no matter how great a surplus of labelled iron may be injected, the dog has almost no ability to excrete this material. Probably these data are enough to indicate why we feel that this method of labelling fed or injected iron with the radioisotope has provided a powerful tool for uncovering the story of iron metabolism. At the present time work is under way on several questions raised by these experiments. Is the iron that appears in the red blood cells as early as five hours after feeding already in the form of hemoglobin?

TABLE I.—RADIO-ACTIVE IRON CONTENT OF TISSUES

Tissue or Organ Content = Per Cent of Total Amount Fed

| | Anemic | | | | | | | Normal | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Dog No. | H-9 | H-8 | 37-116 | 37-227 | | 37-204 | | 37-202 | 37-77 | 37-144 | 37-214 |
| Number of feedings | 4 | 2 | 1 | 1 | | 1 | | 1 | 18 | 5 | 1 |
| Blood volume | 330 | 350 | 500 | 370 | | 440 | | 770 | 480 | 630 | 700 |
| Plasma volume | 260 | 260 | 390 | 250 | | 330 | | 620 | 240 | 360 | 400 |
| Iron fed in mg. | 220 | 66 | 130 | 84 | | 300 | | 115 | 650 | 103 | 60 |
| Counts per minute as fed | 770 | 464 | 5,730 | 21,500 | | 6,590 | | 13,000 | 600 | 2120 | 14,240 |
| Hb. level per cent when fed | 39 | 62 | 53 | 68 | | 61 | | 56 | 178 | 138 | 114 |
| Hours after last feeding | 20 | 20 | 23 | 4 | 75 | 11 | 26 | 6 | 84 | 23 | 7 |
| Radio-iron found in Liver | 0.4 | 0.4 | 0.5 | ... | ... | ... | ... | ... | 0.2 | 0.03 | 0.02 |
| Spleen | 0.0 | 0.0 | 0.1 | ... | ... | ... | ... | ... | 0.0 | 0.02 | 0.01 |
| Marrow | 0.2± | 3.0± | 2.0 | ... | ... | ... | ... | ... | 0.0 | 0.03± | .... |
| Plasma | 0.0 | 0.3 | 0.1 | 0.7 | 0.1 | 0.8 | 0.2 | 3.5 | 0.0 | 0.01 | 0.05 |
| Red cells | 8.7 | 9.0 | 1.4 | 0.9 | 4.6 | 0.0 | 0.4 | 0.2 | 0.04 | 0.06 | |
| Total Radio-iron | 9.3± | 12.7± | 4.1± | 1.6 | 4.7 | 0.8 | 0.6 | 3.7 | 0.24 | 0.15± | 0.08 |

By experiments in which the hemoglobin from blood taken a few hours after feeding of radio-iron is purified and crystallized and

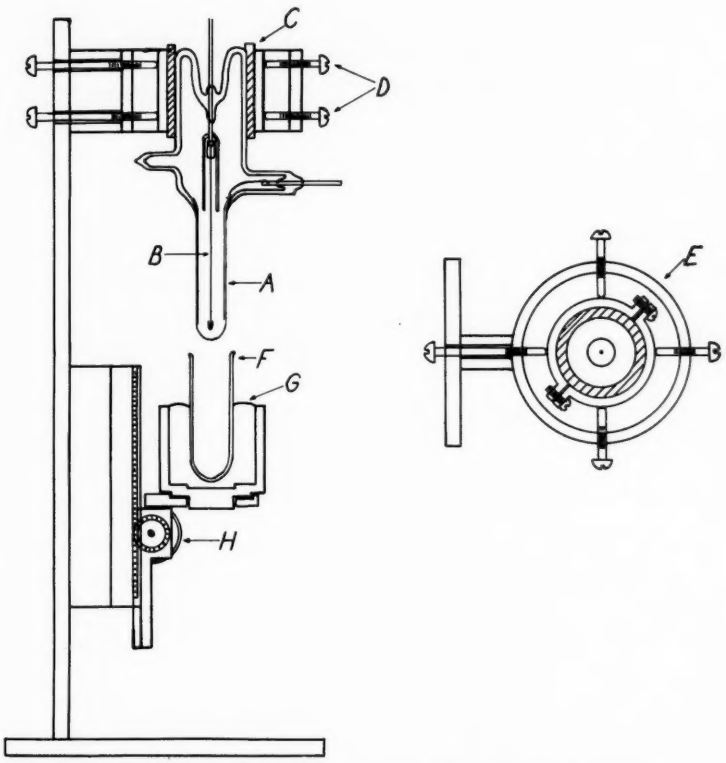



Fig. 2. Geiger-Muller counting tube as mounted for radio-activity measurements. *A*, Sensitive portion of counting tube; *B*, tungsten central electrode; *C*, rubber mounting of counting tube; *D*, machine screws for adjusting tube position; *E*, view from above showing means of clamping counting tube and position adjustment; *F*, glass cup; *G*, paraffin mounting, and *H*, rack and pinion.

its radio-iron content determined, it is hoped to answer this question.

The employment of radio-iron is only one example of how the radio-elements are proving useful as tracers in biologic research. A year and a half ago it would have been quite easy to summarize most of the work that had been done with the radio-isotopes, but to-day that is not possible. One may look only briefly at a few examples of work typical of that now going on.

Unfortunately, although radio-isotopes of the three biologically important elements —carbon, oxygen, and nitrogen—have been prepared, they all have extremely short half lives, the longest—that of carbon—being 20 minutes. This means that with radio-carbon the activity at the end of one hour is down to one-eighth its initial intensity and at the end of two hours, it is down to one sixty-fourth its initial activity.

In spite of this handicap, several groups of researchers have been using radio-carbon in investigations of photo-synthesis. From the University of California, Ruben, Hassid, and Kamen (5) have published the results of some of this work. Their method in general has been, first, to prepare carbon dioxide from radio-carbon and then to expose plant leaves to this atmosphere either in light or darkness. Finally, they meas-

ured the radio-activity of various fractions prepared from the leaf tissue. Thus they are tracing the radio-carbon from carbon

In general though, it seems that the short half lives of these elements make them unfit for most of the experiments using tagged

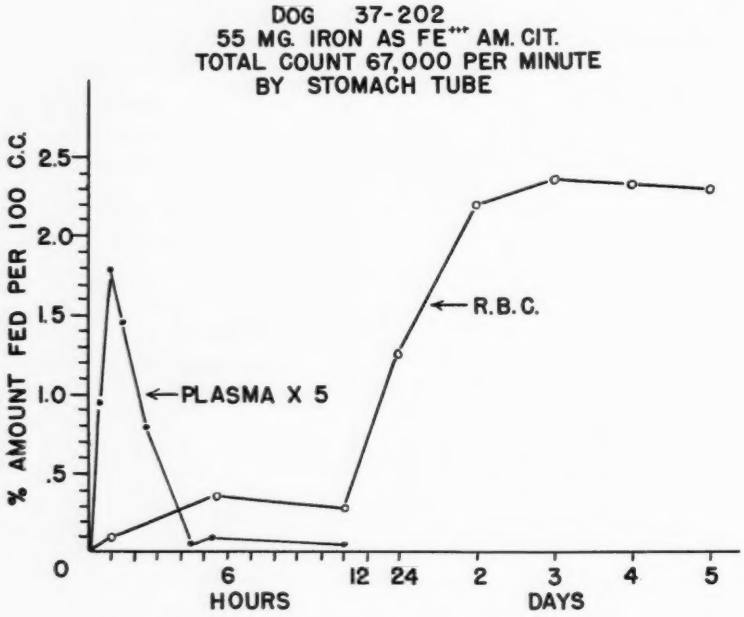



Fig. 3.

dioxide through the chemical changes it undergoes on its path of synthesis into sugars and carbohydrates. One of the interesting results of this work has been to show that, even in the dark, carbon from $CO_2$ is synthesized into organic compounds but that this reaction shortly comes to rest and that sunlight is necessary to obtain the final carbohydrate produce and thus to permit the reaction chain to continue.

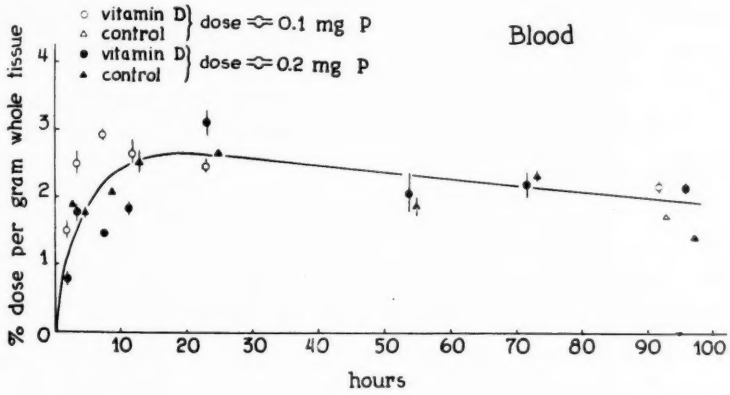
One has a lot of admiration for workers ingenious enough to speed up the complicated determinations of carbohydrate chemistry to the point at which radio-carbon is a useful tool. If much of this work with the short-lived isotopes is done, it almost needs a new name, perhaps "tempo-chemistry."

Radio-chlorine, with a half life of 40 minutes, is being used at the University of Rochester, in some studies on the chloride volume of animals.

atoms that biologists would like to perform. It looks now as if their desire for tagged atoms will be fulfilled by work that Dr. Urey, at Columbia, and other researchers are doing in separating isotopes of elements, work typified by the use to which deuterium (heavy hydrogen) has been put. Nitrogen and oxygen which can be distinguished by their weight have already been prepared and used in preliminary biologic experiments.

Turning now to another radio-active element, some unpublished work that Norton, at the New York State Experimental Station, at Geneva, and Downing, of the University of Rochester, have been doing with radio-active arsenic indicates how a radio-element may be used to carry the sensitivity of chemical analysis to a point that ordinary chemical methods cannot approach. One problem that seems always to confront workers at experimental sta-

tions is that of preparing more potent insect-killing agents for the farmer. In Norton's work on a phase of this problem, the question arose as to how the arsenic in different arsenicals was distributed throughout the bodies of the insects. Due to the small size of the worms with which he was working and the toxicity of arsenic, Norton found that existing chemical methods for this analysis were not sensitive enough. Radio-arsenic can be made in very concentrated form. In this problem, Norton worked with a concentration of about a million counts per minute on the Geiger counter contained in less than a milligram of arsenic. In practice, this meant that he was able to measure quantitatively as little as one-hundredth of a microgram if it were present in an organ dissected from an insect.



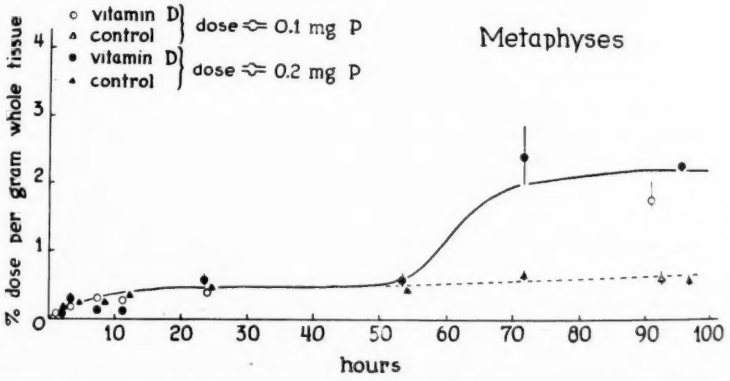




Fig. 4 (*above*). Showing the entrance of radio-active phosphorus into the blood after the administration of a single dose of $Na_2HPO_4$, containing the $P^{32}$ isotope. Note that vitamin D has no effect on the values found after either 0.1 or 0.2 mg. of P.

Fig. 5 (*below*). Showing the retention of radio-active phosphorus in the metaphyseal cartilage. Note that at 72 hours the values in the rats which had been fed vitamin D are significantly higher than in those of the controls.

Papers published so far would indicate that radio-phosphorus has been used as a tagged atom in biologic investigations probably as much as all of the other radio-isotopes together. There are several reasons for this since radio-phosphorus is one of the radio-elements most easily prepared with good activity. Its half life of 14 days is well adapted to biologic work. Also the metabolism and biologic functions of phos-

TABLE II.—CHARACTERISTICS OF RADIO-ELEMENTS USEFUL AS LABELLED ATOMS IN BIOLOGIC RESEARCH

| Element | Half Life | Made from | Bombarding Particle |
|---|---|---|---|
| Phosphorus | 14.5 days | Sulphur | Neutron |
| | | Phosphorus | Deuteron |
| Arsenic | 14 days | Germanium | Proton |
| Sodium | 14 hours | Sodium | Deuteron |
| Iodine | 8 hours and 8 days | Iodine<br>Tellurium | Deuteron<br>Proton |
| Selenium | 40 days | Arsenic | Proton |
| Potassium | 13 hours | Potassium | Deuteron |
| Copper | 13 hours | Copper | Deuteron |
| Iron | 42 days | Iron | Deuteron |
| Sulphur | 84 days | Sulphur | Deuteron |
| Fluorine | 110 minutes | Oxygen | Proton |
| Chlorine | 37 minutes | Chlorine | Deuteron |
| Carbon | 20 minutes | Boron | Deuteron |

phorus and its compounds is one of the fields being investigated most extensively in physiology and biochemistry to-day.

Hevesy, at Copenhagen, was the first to use radio-phosphorus in biologic work, publishing some observations on the metabolism of the phosphate ion tagged with radio-phosphorus, in 1936. Since then, Chaikoff, Greenberg, and co-workers, at California; Artom, in Italy, and Manly and Haven, at Rochester, are among those who have used radio-phosphorus in biologic investigations.

There is one phase of the work with radio-phosphorus that seems of special interest to radiologists, namely, its use in studies of calcification. A review of much of this work is given by Greenberg (6). Some experiments carried out by Morgareidge and Manly, at Rochester, illustrate the use to which radio-phosphorus may be put in experiments of this type. They were interested in the question as to whether the effect of vitamin D in the healing of rickets was due to promotion of phosphate adsorption, or to a local effect on the calcification process in the metaphyseal area. They, therefore, performed a series of experiments in which rachitic rats were fed a dose of one or two tenths of a milligram of sodium phosphate labelled with the radio-isotope of phosphorus (7). In a portion of these animals the labelled phosphorus was accompanied by a single dose of vitamin D. The remaining animals kept as controls were fed only the labelled phosphorus.

Figure 4 shows the labelled phosphorus content of the blood of the experimental and control rats sacrificed at various intervals following feeding. One notes that there is no significant difference in the labelled phosphorus content of the rats fed vitamin D and the control rats. Similar curves made for the labelled phosphorus contents of the long bone shafts of both groups of animals show no significant difference. This is taken by the investigators as evidence that the feeding of vitamin D has had no special effect upon the amount of phosphate absorbed.

Figure 5 shows the results of radio-phosphorus determinations on the metaphyseal portions of the long bones. It will be noted that 72 hours following feeding there is a significant increase in the labelled phosphorus content of this region in the vitamin-fed animals over the controls. The time of this increase of labelled phosphorus is the same as the time of the beginning of the healing of the rickets as shown by the appearance of a positive line test for calcification in the metaphyseal area using a silver nitrate stain in these same animals.

Morgareidge and Manly have interpreted these experiments as indicating a local action of vitamin D at the site of calcification rather than, entirely at least, an influence on phosphate adsorption.

Probably this outline of the types of problems in which the radio-isotopes have proven useful tools up to now is as good a method as any for indicating the types of results that may be expected in the future from the use of the labels for atoms. However, no mention at all has been made of several radio-elements that are being used in biologic research at the present time. Of these the most important are probably radio-sulphur, radio-iodine, radio-sodium, and radio-potassium.

As a summary to this paper, Table II lists some of the characteristics of the radio-elements that at the present time give

promise of the greatest usefulness in biologic research. These elements are listed in an order approximating the ease with which they may be used as radio-indicators in biologic research. Thus phosphorus and arsenic are especially well adapted to use as tracer elements. Using radio-sulphur and radio-iron is difficult because of the low intensities and small beta-ray energies. The short half lives of radio-chlorine and radio-carbon limit experiments with these elements to a few hours at most.

There are alternative methods for preparing several of these elements. In general, the method giving the most active preparation has been listed.

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## DISCUSSION

FRED J. HODGES, M.D., (Ann Arbor, Mich.): There are physicists who find it difficult, if not frankly annoying, to answer the often naïve questions propounded by clinical radiologists, while others, notably our own Quimby, Weatherwax, Failla, Glasser, Thornton, Taylor, *et al.*, are ever most kind and helpful. Surely Dr. Tuve has shown us to-day that he qualifies as a member of this latter group. He has anticipated many of our questions and has attempted to introduce to us the newly developed jargon of nuclear physics.

Most of us are primarily interested in clinical radiology and are apt to be thoroughly discouraged by the fast-moving and intricate theories of modern physics. Dr. Newell has advised us to enjoy what we can understand and to keep on trying to grasp the remainder. His plan has worked fairly well in my case because, although complete understanding is a long way off, I thoroughly enjoy the little that I have absorbed.

It is encouraging and comforting to take the attitude that the physicists, of whom we stand in such great awe, have spent years of their lives perfecting themselves in that field. Much as we might like to transfer our interest at this late date to the subject of physics, that move is wholly out of the question.

Dr. Bale has brought us a glimpse of the truthful literature which, according to Dr. Newell, excels fiction as a form of entertainment. As radiologists we may well be interested readers and listeners insofar as the use of artificially radio-activated tracer substances in biologic experimentation is concerned. At Michigan, we have felt it wise to curb our desires to engage in such work in favor of experiments directly related to the treatment of human disease by radiation methods. If we should attempt to excel in the field where internists, physicists, biologists, and others should find greatest opportunity, we are missing the point of radiology and are apt to lose valuable time and misspend our energy.

Experimentation with tracer substances constitutes a speciality in which the rank and file of clinical radiologists have but little right to trespass. We can learn a great deal from the exploits of others and we may enjoy reading of their accomplishments, but our own efforts will be misplaced if we desert clinical radiology for activities in this field. I, for one, shall be an interested reader of Dr. Bale's material from this date forward.

# TREATMENT OF RADIATION REACTIONS FOLLOWING 200 KV. THERAPY[1]

*By* ZOE ALLISON JOHNSTON, M.D., *Pittsburgh, Pennsylvania*

THERE are a number of conditions to be considered in reviewing the subject of radiation reactions following the use of 200 kv. x-ray therapy.

The treatment may be complicated by the development of radiation sickness, blood changes, skin reactions of all types, from a faint erythema to an ulceration, through stages of desquamation to tanning or bronzing, telangiectasis, or even a fibrosis. Later, there are changes in the deeper structures due to irradiation. Underlying organs are affected. There may be diarrhea or bleeding from the bowel, due to changes in the mucosa of the gastro-intestinal tract. Injuries to the trachea, such as ulceration and fibrosis, are reported. Fractures of bones or the development of cataracts may follow irradiation.

Of these, let us consider the treatment of radiation sickness and of skin reactions. "Radiation sickness" is a term used to cover a syndrome of symptoms characterized by a general toxemia. There is nausea, vomiting, loss of appetite, and a general weakness. These symptoms appear from one to five hours, or longer, after the treatment has been given. One-half or more of the patients treated suffer from radiation sickness to some degree. It may occur when any part of the body is treated, but the degree seems to depend upon the region irradiated, the length of the treatment, and the size of the field.

There are many conjectures as to the cause. Some authors point out that noxious gases, *i.e.*, ozone and nitrous oxide, arising during irradiation, may contribute to the cause. In the past our treatment rooms were poorly ventilated and there was considerable corona and brush discharge from the old type of apparatus. Many patients were really sick. Now, even with well ventilated rooms and the new type of machines, our patients still suffer from radiation sickness. One explanation for this is the fact that we are giving larger total doses than formerly, and since the patients are treated every day or every other day, they do not have time to recover from the sickness between treatments. The main cause is evidently some type of general reaction which seems to be metabolic in nature.

We know, from investigations of various authors, that there is a disturbance of the chloride metabolism and in the cholesterin content of the blood. There is, contrary to former beliefs, an alkalosis.

Schreus and Willms found that there was an increase of beta-oxybutyric acid in the blood and, to a lesser extent, an increase of acetic acid. This preceded roentgen sickness following irradiation. It seemed reasonable, too, that the condition should be cured or prevented by agents which overcome acetonemia. These investigators reported excellent results with the use of insulin.

Jugenberg stated that there was an imbalance of the bacteriology of the colon and that radiation sickness was due to resorption of products of decomposition. There was a decrease in the number of *Bacilli coli*, and an increase in other bacteria. She reported 43 patients treated with coli sour milk, with marked decrease in radiation sickness.

Burgheim reported 70 cases of roentgen sickness, in all of which the blood cholesterin was found to be low. These patients were treated with colsil (a cholesterin preparation) with marked success.

Schneider reported good results in 100 cases treated with colsil in which the effects were similar to Burgheim's.

Cameron and McMillan found that roentgen-ray therapy in massive doses

[1] Read before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

produced a definite lowering of urinary excretion and a definite chloride retention when the upper abdomen was irradiated. Preliminary feeding of sodium chloride daily, so that the chloride excretion was raised to 10 grams more per day before treatment, and its use during treatment prevents or lessens the sickness. Blood chloride was not always affected. There was usually a slightly greater nitrogen excretion.

Doub, in reporting the results of some experiments, states that the administration of ammonium chloride, sodium chloride, and hydrochloric acid does not give relief, although calcium chloride, calcium lactate, and morphine are beneficial.

Richards and Peters report the use of nembutal with satisfactory results.

Friedman and Drinker suggest the use of the gas mask or respirator, reporting good results therefrom.

The use of liver extract has become popular, but this is not a new suggestion, its use having been advocated previously in Germany and in England. The results from this treatment seem to be far superior to those of any other medication. Barton Young reported a series of cases in which there were spectacular results in 53 per cent of the cases, good results in an additional 23 per cent, while in 24 per cent the use of liver extract was considered to be a failure.

The results in the treatment of radiation sickness by the use of liver extract given by mouth have not been as satisfactory as when it has been given intramuscularly or intravenously We give liver by mouth frequently, and, since many of our patients are from rural districts, we refer a number of them to the local physician for intramuscular injection of liver extract, following which about 50 per cent have shown improvement.

The next development was the use of vitamin $B_1$. During some experimentation with animals, it was found that lack of, or, rather, depriving the animals of, vitamin $B_1$ produced a syndrome of symptoms similar to radiation sickness. This stimulated interest in the use of this medication, and many clinics began using it with marked success. Martin and Moursund reported the results of some experimentation with animals, and brought up the problem as to whether roentgen intoxication resulted in avitaminosis or if the improvement in the vitamin-fed animal was due to the stimulation of the appetite and maintenance of good physical condition. Some had suggested that the intoxication resulted from lack of absorption of vitamin $B_1$ due to a damaged intestinal tract, but that did not seem likely, since relief of symptoms was obtained when the medication was given by mouth.

It is difficult to dissociate reaction due to effect of radiation on the gastro-intestinal tract from radiation sickness. Desjardins reviewed this subject quite thoroughly, in 1931, and concluded that heavy treatment over the gastro-intestinal tract produced about the same symptoms as roentgen sickness, with the addition of tenesmus and diarrhea. He found that the intestine was much more sensitive to direct irradiation than the stomach, and the small intestine much more sensitive than the colon. He also found that the effect on the mucosa of the gastro-intestinal tract was separate from that on the lymphatic glands of the gastro-intestinal tract. The conclusion about this particular part of his review was: "The clincial disturbances caused by excessive irradiation of the bowel constitute a specific reaction, which, although of the same general character as the common non-specific reaction known as radiation sickness, differs essentially from it and is a separate and distinct process."

These deductions are borne out by Palmer and Templeton, who had an opportunity to observe the mucosa of the stomach at operation after x-ray therapy for peptic ulcers had been given. Definite changes in the tissues due to radiation were observed. Some of their patients suffered from radiation sickness but this usually disappeared after two or three treatments.

An article by Arons and Sokoloff on the rôle of the reticulo-endothelial system in

cancer appeared in a recent issue of the *American Journal of Roentgenology and Radium Therapy*. This system (reticular tissues, in general, and the phagocytic cells of the spleen, pulp, marrow, lymph glands, and Kupffer cells of the liver, in particular) is regarded as being concerned with the defense of the body against living and non-living toxic agents, either by the process of antitoxin formation or by phagocytosis. These reticular elements are distributed over the entire body. These tissues are extremely sensitive, and the balance is easily disturbed. Radiation therapy disturbs this balance. A small dose stimulates the reticulo-endothelial system, increasing its protective properties, and a large dose inhibits or destroys its defense mechanism.

A search was made for a substance which might act as a stabilizer of this system. The effect of Congo red, a mono-azo dye, upon the reticulo-endothelial system was studied. The experiments extended to the field of inter-relation between the activity of the reticulo-endothelial system and the resistance to malignant disease. The activity of the reticulo-endothelial system can be tested by its absorptive properties. From 80 to 100 c.c. of a 1 per cent solution of Congo red injected intravenously is almost immediately eliminated from the blood by the liver and spleen. Irradiation of the spleen, one hour previous to the injection of the dye, produces more rapid elimination of the dye. Congo red has been used as a coagulant, having been used with success in cases of hemorrhage due to tuberculosis and cancer. In all of the cases in which it was used, there was no toxic effect. The authors feel that roentgen sickness is only one symptom among others which shows the disturbance of the reticulo-endothelial system. They are convinced that this preparation may be of some value in these cases. The mere fact that the dye is harmless and has some inhibiting effect on the growth of some tumors, as well as a stabilizing effect on the reticulo-endothelial cells, suggests the value of its application.

Early blood changes are closely related to radiation sickness. The director of a commercial pharmacologic research laboratory became interested in this subject and drew conclusions from phytopharmacologic examinations of blood serum in a number of animals. Certain toxins can be demonstrated in the blood and it becomes possible to determine the phytotoxic index.

The degree of toxicity depends upon the species of animal and upon the dose given, but it was greater in 24 hours than immediately after the treatment. Various parts of the body were exposed and the results tabulated. There was the greatest toxicity when the head was irradiated, the abdominal region was next, and the thorax the last to be affected.

The question arose as to whether or not there were any pharmacologic means of preventing radiation sickness, and a number of recommended substances were tested. Among these were Congo red and vitamin $B_1$. The toxic index was not changed when Congo red was used, but vitamin $B_1$ definitely reduced the toxic index.

This review of these treatments suggested for radiation sickness gives an idea of the variety of remedies which have been mentioned. Results reported by one author have not been duplicated by others in many instances. Some radiologists feel that the solution of this problem is simple, believing that the quantity of radiation given to the patient determines the amount of radiation sickness, and that, therefore, if the dose is reduced, the patient will not suffer from such sickness. This suggestion is not practical when patients are coming into an office from a distance. Reducing the dose interferes with the administration of an outlined series of treatments. In our own work, vitamin $B_1$ seems to be the medication which offers the most relief to our patients. In extreme cases, vitamin $B_1$, with the addition of small doses of nembutal, has given satisfactory results.

Unfortunately, in order to give a lethal dose to some underlying part of the body,

certain changes occur in the sebaceous and sudoriferous glands, hair follicles, and other portions of the skin.

I have mentioned the various degrees of reaction, and from the standpoint of treatment these may be divided into early and late reactions. Many radiologists feel that the early reactions should be left alone; our impression is that the patient is happier and more contented if some treatment is given. However, it is true that it should be as simple as possible.

First of all, every patient receiving treatment should be warned not to apply any medication to the area treated. The patients should be warned especially to avoid applications of adhesive plasters, mustard plasters, musterole, iodine, heat, or any medication for rheumatism. If the patient is prepared mentally to expect the gradual appearance of a reaction, when it appears he will not be alarmed. We recommend the use of a lotion containing zinc oxide or calamine, which not only soothes but covers the reaction.

If the reaction is severe, the patient is uncomfortable and many times unable to sleep. A sitz bath for pelvic cases, or an ice bag for other parts of the body, with a mild sedative, is quite comforting. Dry powder—stearate of zinc—may be used. If the skin breaks and dry crusts form, the patient is many times more comfortable if an ointment is used; otherwise, we avoid greasy applications.

These reactions all heal unless there has been carelessness in omitting the filter, or bad judgment in estimating the dosage. In such instances, deep ulceration may follow. The whole leaf of the *Aloe vera*, or some preparation of this, is highly recommended for relief of burning and pain. Narcotics may be necessary during the acute stage. Later, if healing is delayed beyond a reasonable length of time, surgical measures become necessary.

The late skin reactions following x-ray therapy are usually telangiectasis or fibrosis. If the telangiectasis involves an unexposed part of the body, treatment is not necessary. If there are a few dilated vessels on an exposed part of the body, the electric needle or electric desiccation will destroy them, but if a large area is involved some type of plastic surgery is necessary. Since the sebaceous glands are destroyed, it seems reasonable to advise patients to apply some greasy or oily application.

There are few references to this subject in the literature. A French article on radiodermatitis and active ulceration treated and cured by halibut liver ointment was recently abstracted in this Journal. The analgesic anti-infectious and healing properties of fish liver oils of high vitamin A and D content are well illustrated by results in a series of cases of radiodermatitis and of ulcerations from other causes treated with local applications of haliver oil.

No doubt, each radiologist has his own scheme or plan for the treatment of these cases, and discussion might be of interest and benefit to all of us. When using x-ray therapy, every precaution should be taken to protect the patient. We must guard against accidents due to carelessness, or incorrect estimation of a proper dosage, and we must provide adequate protection to surrounding tissues as well as to underlying tissues and organs.

The warning is old, but it bears repetition. Irradiation is a powerful agent which should be used only by those trained to recognize its dangers as well as its benefits.

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DISCUSSION

LOWELL S. GOIN, M.D. (Los Angeles): I am sure that you agree that Dr. Johnston has given us a practical presentation of a subject of the most immediate daily importance to all of us.

I think it is important to remember that when we apply large amounts of radiation to the human body, there are two groups of symptoms which result. These are divided, as Dr. Johnston has indicated, into the general systemic reactions which we know as radiation sickness, and the local effects; and we must not forget that the local effects can be either external or internal and that it is likely that the proctitis, the cystitis, the sigmoiditis, and whatnot that our patients complain of are only the internal local effects, and are not an immediate part of the problem of radiation sickness.

It is to the latter problem that I would like to confine my few remarks.

There is only one treatment for diphtheria and I suppose there have been a thousand proposed for epilepsy. Whenever we see that situation obtain it is because we do not know much about the condition for which we are proposing the treatments.

That is probably the reason why there is such a large number of treatments proposed for radiation sickness and it is also likely that radiation sickness is the result of multiple causes, so that a therapist in one place may report excellent results from the use of liver therapy while another finds it is not so useful. Perhaps the explanation is that the patients being treated do not have radiation sickness resulting from exactly the same causes.

There is a certain plausibility to vitamin deficiency as a cause for radiation sickness. Most of our patients, of course, are suffering from malignant disease; they are largely undernourished (at least the ones that I see are), a great many having already been attracted to faddist diets in the hope of controlling their disease so that they have the stage naturally set for a vitamin deficiency.

Certainly the administration of vitamin $B_1$ in the form of thiamin chloride relieves many of these patients. Vitamin deficiency is a thing that has accumulated over a considerable period of time and it will not yield to the administration of a few vitamin $B_1$ tablets by mouth, or at least it never has in my experience. When I use vitamin $B_1$, I use 100 mg. of thiamin chloride intravenously on alternate days until the patient's symptoms are either controlled or it is apparent that they are not going to be controlled.

As a usual rule, 300 mg. of thiamin chloride will either control the symptomatology or convince you that it will not be controlled.

However, there must be causes of radiation sickness other than vitamin deficiency, and, in an attempt to establish those causes, all of us have had blood chemistry studies done and have made what investigations we could. We have not found any

disturbance in the blood cholesterol or in the non-protein nitrogen contents of the blood or in the blood sugar. We have occasionally found the blood chlorides reduced, but we think that our most significant finding (in a very small group of cases) is a decrease in the carbon dioxid combining power of the blood plasma. The carbon dioxid combining power is an index of the sodium level of the blood plasma and of the amount of sodium free in the blood to combine with the acid radicals and is the index of the likelihood of the patient to develop acidosis.

We have seen the $CO_2$ combining power, normally between 50 and 60, as low as 18, and we have been able to relieve promptly the symptoms by the intravenous administration of a so-called "molar" solution of sodium lactate. If a sufficient number of patients are thus treated with success, we probably will have found one answer to the problem of radiation sickness.

A molar solution of a substance is made by dissolving the molecular weight of the substance in grams in 1,000 c.c. of water; and we have a very exact method of administering the molar solution.

The amount of sodium lactate, which is an excellent source of sodium for the blood plasma, necessary to raise the sodium level to its normal, can be rather exactly determined by subtracting the carbon dioxid combining power from 60 and multiplying by three-tenths of the patient's weight in kilograms. The resulting figure represents the number of cubic centimeters of a molar solution of sodium lactate needed to restore the sodium level to theoretic normal.

Although the number of cases we have thus treated is so small as to be of no consequence whatever, I believe that, in some cases, at least, we will be able to secure prompt relief by the administration of this form of therapy.

# PHYSICAL FACTORS OF LOW VOLTAGE "CONTACT" ROENTGEN THERAPY[1]

*By* CARL B. BRAESTRUP *and* IRVING HANSON BLATZ, *New York City*

From the Physical Laboratory, Division of Cancer, Ira I. Kaplan, M.D., Director; Department of Hospitals, City of New York

MOST of the improvements in radiation therapy have been instituted with the aim of increasing the dose to the lesion without causing any harmful effects to the healthy tissue. In irradiating surface conditions and those accessible through the cavities of the body or through operative procedure this object may be attained by using rays at shorter skin–target distance and of longer wave lengths, that is, of less penetrability, thereby reducing the dose to the underlying normal tissue.

Until recent years, before the advent of shockproofing, it has not been possible to reduce materially the target–skin distance with safety. The so-called Grenz-ray tube was devised by Bucky to permit operation at from 10 to 12 kv., using an 8 to 10 cm. distance, yet its use is limited to the treatment of only the most superficial layers of skin as the depth dose is only about 15 per cent at 1 mm. depth.[2] Furthermore, the necessity of making the x-ray tube wall extremely thin to minimize inherent absorption makes the apparatus very delicate for general use.

About six years ago Chaoul and his co-workers (1) devised another method of low voltage irradiation. They used the following factors: approximately 50 kv. constant potential, a filtration equivalent to about 0.2 mm. Cu, and a target distance of from 2 to 6 cm.

The short target distance was made possible by the development of a new type of x-ray tube in which a gold-plated nickel target is mounted at the extreme end and serves as both target and filter. Measurements using this type of tube have been described by Mayneord (3) in some detail, and also by Pendergrass, Hodes, and Garrahan (2). More recently another type of low voltage tube with greatly reduced inherent filtration has been devised. Inasmuch as this type has received considerable attention in this country, we have made a study of its physical and technical characteristics. The construction of both types is shown in Figure 1 for comparison.

*Equipment.*—The measurements were carried out on seven constant potential, single valve, low voltage contact therapy units, all of the Philips type. The negative terminal of the generator was grounded, while the other was connected through an insulated, shielded cable to the anode of the x-ray tube. One side of the filament, as well as the outside metal shell of the x-ray tube, was grounded and the x-ray tube was cooled by means of forced air circulation. It will be observed that in contrast to the Chaoul type tube described by the other investigators this x-ray tube has a very low inherent filtration as its useful beam does not pass through the target.

*Measuring Instruments.*—A 12.5 cm. sphere gap calibrated with one side grounded was used to determine the crest voltage. A Taylor type high voltage resistance unit (4) was used to measure the effective voltage, and the ripple was checked strobographically, using a photoelectric cell densitometer to analyze the film. The stray radiation was determined by means of a large ionization chamber previously described (5). The other ionization measurements were made by means of three different types of thimble chambers, the smallest one of which had an inside diameter of 4 mm. and a volume of 0.05 c.c. All the chambers had previously been calibrated against our standard open air

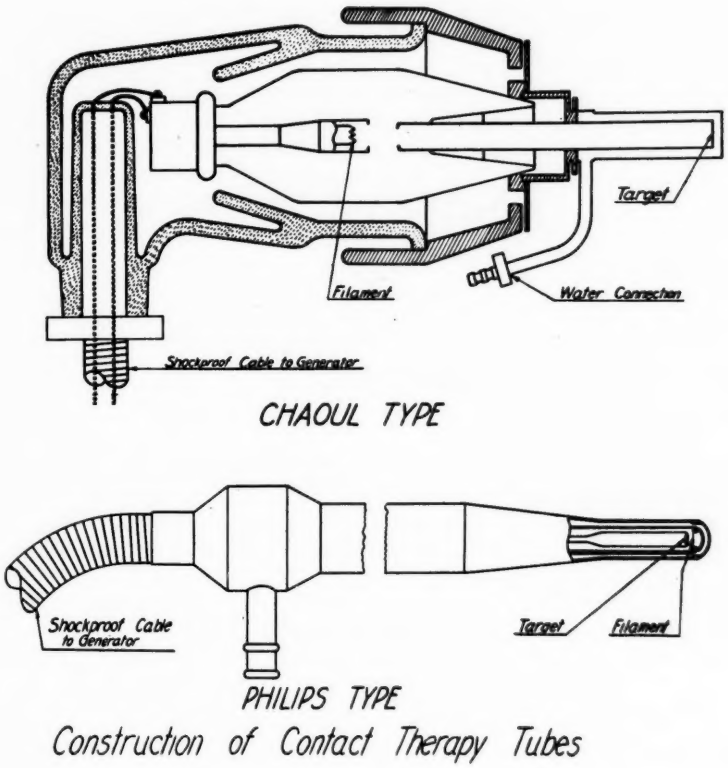
[1] Presented before the New York Roentgen Society, Academy of Medicine, May 15, 1939.

[2] The tube voltage more recently has been increased to 25 kv. with resultant improvement in depth dose.

chamber. During the experiments the x-ray tube was mounted on an adjustable tube bench which permitted accurate adjustments of the target distance by means of a calibrated worm screw arrangement, as shown in Figure 2. The ionization chambers were connected to either a string type electrometer or a direct current amplifier. The depth dose measurements were carried out using laminated "Masonite"[3] and checked with a water phantom.

*Experimental Procedure.*—First the crest voltage across the x-ray tube was determined by means of the sphere gap and found to be 44 kv. at 2 ma. This value was checked by means of the 100 megohm resistance unit and a microammeter connected in series across the x-ray tube connections at generator. The x-ray tube current was reduced by the amount drawn by the resistor, 0.42 ma., in order that the total current drawn from the generator be equal to the normal milliamperage of 2. The current, 0.42 ma., through the 100 megohm resistance represents an effective tube voltage of 42 kv., making the ripple 4.8 per cent. This value, checked strobographically, gave a net density ratio of from 0.51 to 0.66, or a ripple of 5.8 per cent obtained from the square root of the ratio of the net densities for unfiltered radiation at the crest and the trough of the wave.

The focal spot image (Fig. 2) was obtained by means of the pinhole method, using a 0.5 mm. diameter hole, a distance




Construction of Contact Therapy Tubes

Fig. 1.

[3] "Masonite presdwood" is a wood fiber board obtained by exploding wood chips by high pressure steam. These fibers are then pressed into board form in steam-heated hydraulic presses. The density of the type used in this work is unity.

2 × 10 cm., and 40 sec. exposure. Roentgenographs of the tube were made with roentgen and gamma rays to determine the exact location of the target; it was found to be 1.8 cm. from the outside surface of the cap. The relation between the field size and the target distance was also established roentgenographically. The field was found to be circular with a diameter equal to 1.36 times the target distance.

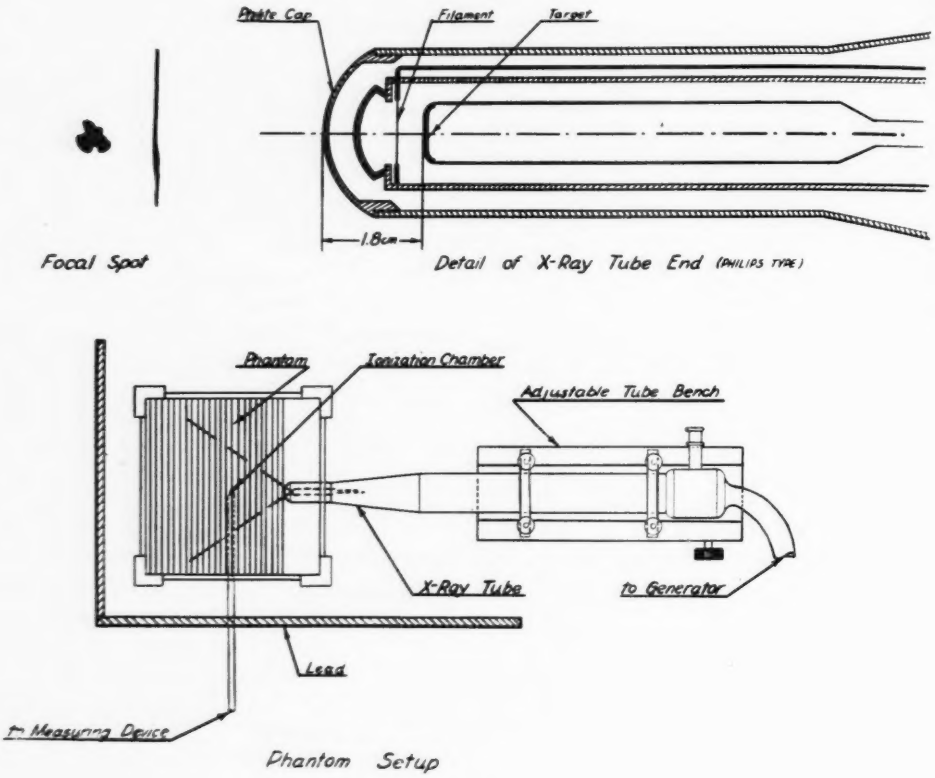



Fig. 2.

Ionization measurements were made of the dosage rate in air at various target distances to determine whether the r/min. varied inversely as the square of the distance or some correction factor would have to be applied. There are two factors which might affect this relationship: (*a*) the fact that the focal spot is not a point, and (*b*) the absorption in air. As indicated on Figure 3, the results plotted on log-log paper show that within the range of the measurements the ionization varies closely with the inverse square of the distance and, in general, it is not necessary to make any correction for air absorption or size of focal spot.

Next, absorption curves were determined in aluminum, as shown in Figure 4. It will be observed that there is little change in the slope of the curve for unfiltered radiation after about two millimeters of aluminum and, consequently, any additional filtration will not materially improve the quality of the beam as practical homogeneity has been reached. With an initial or equivalent filtration of copper as used by Chaoul, there is a rather sharp initial bend due to the absorption of the soft

characteristic radiation of the copper by the first 0.5 to 1 mm. of aluminum. This indicates the need of an auxiliary filter equivalent to at least 0.5 mm. aluminum to obtain the full advantage of the copper filtration. This is further verified by the depth dose measurements which show that the auxiliary filter also improves the depth dose considerably. In the Chaoul type tube, the cooling water in front of the target acts also as auxiliary filter.

The depth dose was determined with the arrangement shown and checked with a water phantom. Because of the high dose gradient with respect to depth, it was essential that the smallest ionization chamber (4 mm. diameter) be used. Measurements were made at the surface and in the depth in steps of 5 mm. The results, expressed in percentage of the surface dose and at the center of the field, are plotted semi-logarithmically in Figure 5. In this

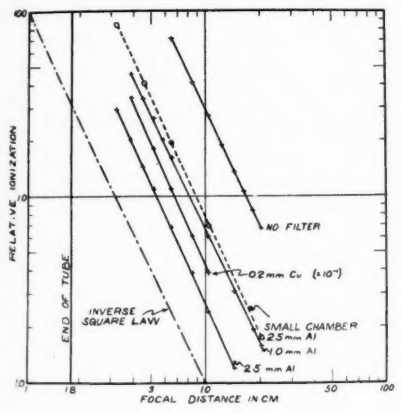



Fig. 3.

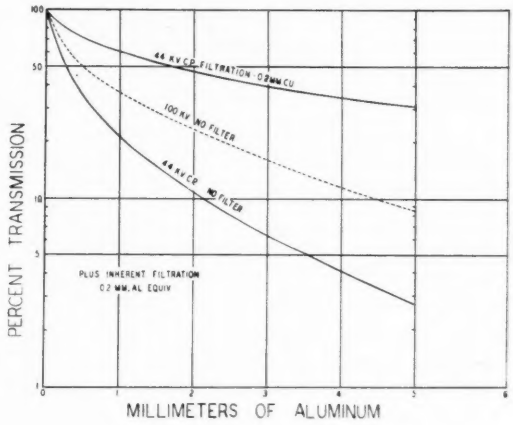



Fig. 4.

Fig. 3. Comparison of experimental data with the inverse square law.
Fig. 4. Absorption curves.

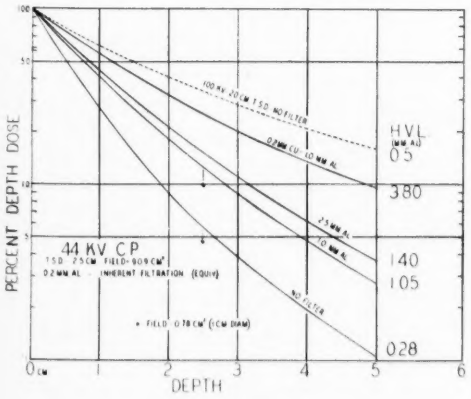



Fig. 5.

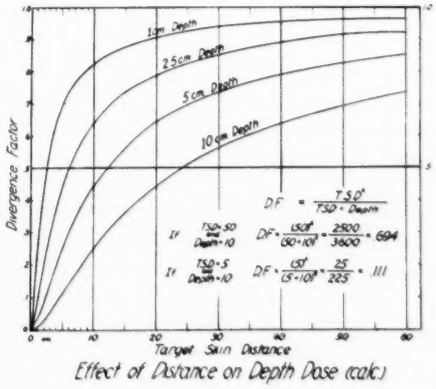



Fig. 6.

Fig. 5. Effect of filtration on depth dose (2.5 cm. T.S.D.). Curves of depth dose measurements using masonite phantom. Comparative measurements made with water gave slightly lower values. Masonite, however, was used as it permitted more accurate duplication of setup.
Fig. 6. Effect of distance on depth dose (calculated).

chart is shown the effect of filtration on the depth dose at a fixed target distance of 2.5 cm. The curves indicate that the first millimeter of aluminum filter improved the depth dose considerably, while any further increase in aluminum filtration shows but little additional gain. The use of much greater filtration by Chaoul was by necessity rather than by choice. As previously shown, his tube has a high inherent filtration. On this diagram is also shown the effect on the depth dose of reducing the field size by means of diaphragms.

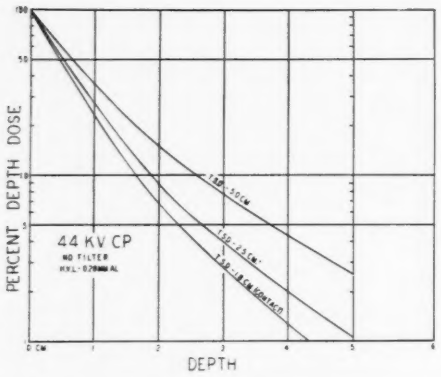



Fig. 7. Effect of distance on depth dose.

The very small depth dose obtainable with "contact" technic is not so much due to the low voltage, but, rather, to the short target–skin distance. To illustrate this point a series of curves show in Figure 6 the "divergence factor"; that is, the depth dose obtainable if there were no absorption or scattering in the tissue. These curves, obtained by calculations using the inverse square law, emphasize the significance of the target–skin distance on the depth dose. This chart may also be used to calculate the approximate depth dose at any distance if known at some other distance and all the other factors remain the same. This may be evident from our phantom measurements made at different target–skin distances as indicated in Figure 7. A comparison of divergence factors with our phantom measurements made with different target–skin distances shows that the depth dose may be obtained by multiplying the divergence factor by a constant. This constant, characteristic of the radiation quality and field size, corrects for the absorption and scattering in the tissue.

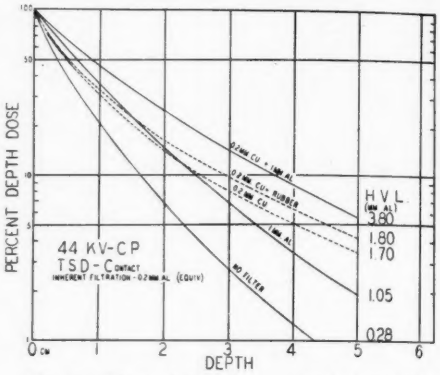



Fig. 8. Effect of filtration on depth dose (tube in contact).

When the x-ray tube is used in actual contact, the target distance depends upon the filtration used, as the filter is placed between the tube end and the skin of the patient, in contact with both. Measurements were made at contact distance and the results are shown in Figure 8. The improvement in the depth dose for the filtered radiation is here obviously due not only to the improved ray quality but also to the greater target distance. The same results are shown in tabulated form in Table I, in which, for the purpose of comparison, two common superficial therapy technics are included. It is apparent that, in cases in which it is desired to irradiate only the more superficial layers, the contact technic is preferable, provided the area to be treated is small.

In addition to the equipment investigated in our laboratory, through the courtesy of the manufacturer, we have made standardization measurements of six other units, all of the same type. A comparison of their dosage rate is shown in Table II. As might be expected, there is some variation in the unfiltered radiation output, due to the difference in inherent filtration

in the tube wall and cap. As the filter is increased, the significance of the inherent filtration is reduced, explaining the greater uniformity. The exceedingly high dosage rate for unfiltered radiation is due solely to the short distance. As indicated in Table II, the r/min. at 20 cm. is much less than that ordinarily obtained at this distance with 100 kv., 3 ma., and no filter.

*Stray Radiation.*—The introduction of new apparatus or technics always requires due consideration of the question of x-ray protection. Accordingly, measurements were made to determine the amount of stray radiation the operator or attendants would receive These tests were made with and without the protective lead glass disk provided to minimize secondary stray radiation from the patient. Measurements were made with the tube end in contact with a scattering medium. The results are shown in Figure 9.

In addition to these measurements, tests were made without a scattering medium in place. Results showed that without the shield in place about 80 to 90 per cent of the stray radiation was secondary rays from the scattering medium. In evaluating the significance of the stray radiation figures, due consideration must be given to the actual cumulative treatment time and low penetrability. On account of the high dosage rate to the patient, the treatment time is usually extremely short in comparison with conventional technics. If the total daily treatment time without filter exceeds seven and one-half minutes, with the tube held by the operator for external irradiation, it is necessary that a protective shielding or lead rubber gloves

TABLE I.—PERCENTAGE DEPTH DOSE

| Filter[1] | 44 kv. at "Contact" Distance | | | | | | 100 kv. (at 30 cm.) | 135 kv. (at 30 cm.) |
|---|---|---|---|---|---|---|---|---|
| Cu | 0 | 0 | 0 | 0.2 | 0.2 | 0.2 | | |
| Al | 0 | 1 | 2.5 | 0 | Rubber | 1 | 0 | 3 |
| H.V.L. (mm. Al) | 0.28 | 1.04 | 1.40 | 1.75 | 1.80 | 3.8 | 0.5 | 5.1 |
| Diam. of field | 2.45 cm. | 2.86 cm. | 2.86 cm. | 2.86 cm. | 2.86 cm. | 2.8 cm. | 14 cm. | 14 cm. |
| Surf. | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |
| 1 cm. | 23.0 | 36.3 | 40.1 | 31.0 | 32.3 | 46.6 | 66.9 | 92.0 |
| 2 cm. | 6.7 | 14.4 | 17.9 | 13.9 | 16.2 | 24.3 | 44.2 | 79.5 |
| 3 cm. | 2.7 | 6.7 | 9.0 | 8.0 | 9.7 | 14.1 | 31.2 | 68.0 |
| 4 cm. | 1.2 | 3.4 | 5.1 | 5.1 | 6.2 | 8.7 | 23.4 | 58.0 |
| 5 cm. | 0.6 | 1.9 | 3.0 | 3.4 | 4.2 | 5.5 | 18.4 | 49.5 |

[1] Plus inherent filtration of tube wall.

TABLE II.—COMPARISON OF DOSAGE RATES OF DIFFERENT CONTACT THERAPY UNITS, PHILIPS TYPE OPERATING AT 44–50 KV. CONSTANT POTENTIAL AND 2 MA.

| Unit | r/min. (in Air) for Different Filters[1] and Target Distances | | | | |
|---|---|---|---|---|---|
| | No Filter | 1 mm. Al | 2.5 mm. Al | 0.2 mm. Cu 1 mm. Al | No Filter |
| | 1.8 cm. | 2.1 cm. | 2.1 cm. | 2.1 cm. | 20 cm. |
| MCH-1 | 9,800 | 1,590 | 704 | | 79 |
| MCH-2 | 7,940 | 1,695 | 732 | | 64 |
| JTM | 9,500 | 1,590 | 644 | 275 | 75 |
| PL | 9,500 | 1,470 | 555 | 245 | 75 |
| WH | 6,470 | 1,330 | 533 | | 52 |
| MH | 10,650 | 1,810 | 703 | | 86 |
| MSH | 9,250 | 1,730 | 680 | | |

Average r/min. at 100 kv., 3 ma., no filter equals 225 at 20 cm.
[1] Plus inherent filtration of tube wall and cap (equivalent to approximately 0.2 mm. Al).

and apron be used in order to keep the stray radiation below 0.2 r per day to the body of the operator. If filter or diaphragms are used, this time may be increased accordingly. In case of cavity application the stray radiation is in most cases negligible.

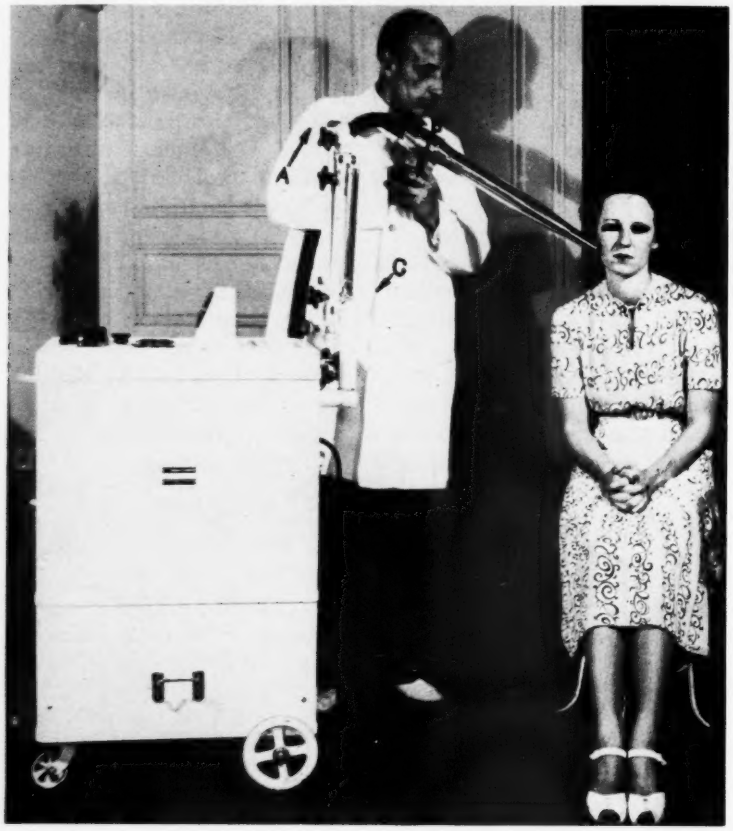



Fig. 9. Stray radiation in r/min. (no filter—no diaphragm). *A*, a point adjacent to the tube cable at one meter back from the tube end; *B*, at the handle on the tube holder (position of operator's hand if tube is being held) at 55 cm. from tube end; *C*, a point at one meter from the tube end but in a direction 45 degrees from the tube axis. A = 0.02 r/min., B = 0.08 r/min., C = 0.03 r/min.

*Discussion.*—It may be of interest to compare the physical factors of the two types of x-ray tubes which are at present available for low voltage short distance irradiation, namely, the water-cooled tube used by Chaoul and the air-cooled Philips type discussed in this paper.

Using Pendergrass' data for the Chaoul tube, both types were operated at almost identical voltage, about 45 kv. constant potential. As the Chaoul tube is water-cooled, its milliampere rating is higher, that is, 4 ma., or twice that of the other type. However, at equal distances and without any external filter the dosage rate per milliampere of the Philips tube is about 25 times as great, due to its low inherent filtration. On the other hand, if 0.2 mm. Cu plus 1 mm. Al is added to this tube to equalize the filtration of the two x-ray tubes, the r per milliampere-minute is about the same for both. Yet, at 45 kv. the ray quality of the air-cooled

tube is higher; it has a H.V.L. of 3.8 mm. Al against 2.4 for the water-cooled type. Apparently, the inherent filtration of the Chaoul tube is equivalent to 0.2 mm. Cu plus 1 mm. Al only quantitatively but not qualitatively. It should be pointed out that the voltage rating of both types of x-ray tubes, that is, 50 to 60 kv., is at present the maximum, permitting a tube construction compact enough for intercavity application. As indicated in Table I, this voltage offers sufficient penetrability for the present field of applications. The short target–skin distance principle may be used to advantage also with higher voltages, although generally 10 cm. is then the closest distance possible.

One of the outstanding characteristics of contact roentgen therapy is the possibility of approximating the depth dose obtainable with radium. For instance, a 20 mm. long radium tube with 0.5 mm. Pt filtration applied at 7 mm. skin distance will give the same depth dose 1 cm. below the surface as with unfiltered contact roentgen therapy. However, it would be practically impossible to duplicate the high x-ray dosage rate as it would require about 35 grams of radium. Similarly, a non-uniform surface dose distribution is obtained with both technics on account of the dose diminution toward the periphery of the field.

The surface dose falls off more rapidly, as we depart from the center of the field, than can be accounted for by the increased linear distance from the target. This may be explained by the shape of the target. Along the axis of the tube (central beam), part of the radiation received originates at the conical part of the target. As we approach the periphery of the field, the angle on one side becomes correspondingly less and soon a cut-off point is reached at which the radiation drops off sharply. The geometric layout is shown in Figure 2.

In cases in which caustic irradiation (6) is desired, the depth dose (in terms of the surface dose) is of little significance. In such cases it is more important to know the dosage rate at the different depths in the tissue so that the lethal dose may be predetermined at the desired level and, consequently, filtration would only reduce the output.

On the other hand, if it is desired to reach the deeper tissue with the least damage to the skin (or surface), from 1 to 2 mm. of aluminum filter should be used to obtain a more homogeneous radiation (7).

The unusually high dosage rate and the relatively low depth dose characteristic of this technic may be ascribed to the short target distance. As shown by our measurements, the ray quality of the equipment differs only slightly from conventional unfiltered low voltage technics. The apparatus offers a convenient means of approximating the dose distribution obtainable with radium; the dosage rate, however, is so much higher.

The high dosage rate necessitates extreme precautions, as an erythema dose may be delivered in a few seconds. Accurate timing and close supervision are, therefore, essential.

We wish to express our appreciation for the helpful advice given by William Harris, M.D., and the assistance rendered by Mr. Gordon Cameron and Mr. O. T. Smith.

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# NORMAL BONE ANGLES AND THE ROENTGEN REPORT[1]

*By* R. G. VAN NUYS, A.B., M.D., *Berkeley, California*

AN orthopedist confided to me recently that there was often considerable variation in roentgenologists' reports, and that they were frequently indefinite. For example, a report might read "good alignment," "fair alignment," "some angulation," etc. How then, should we, as roentgenologists, report our fractures? Can we not make our reports more definite by stating variations from the normal in angles and centimeters?

[1]Read before the California Medical Association, Section on Radiology, at the Sixty-seventh Annual Session, at Pasadena, May 9–12, 1938.

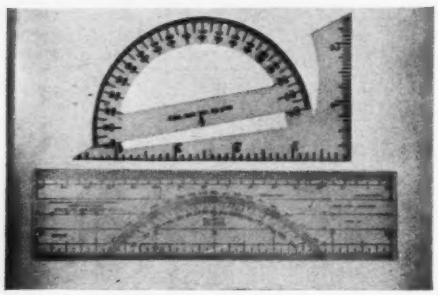

Fig. 1. Sample rulers. The central point may be placed at the apex of the angle and the degrees noted.

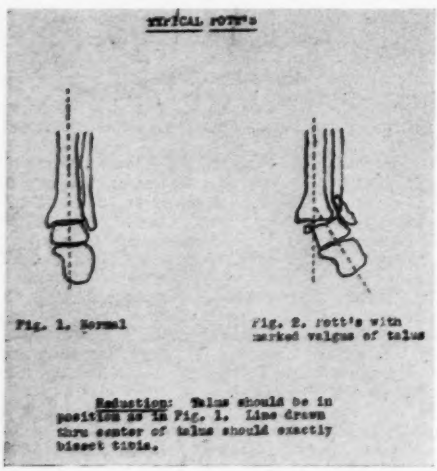
TYPICAL POTT'S
Fig. 1. Normal
Fig. 2. Pott's with marked valgus of talus
Reduction: Talus should be in position as in Fig. 1. Line drawn thru center of talus should exactly bisect tibia.

Fig. 2. In Figure 1 (*above, left*) the line drawn through the center of the tibial shaft passes through the center of the os talus. In Figure 2 (*above, right*) there is a 32-degree valgus.

Frequently doctors have asked me what an angle should be normally, to which question I have addressed my efforts. I have studied numerous films of wrists, elbows, shoulders, hips, knees, ankles, and feet, and recorded measurements of angles in normal and pathologic cases. I shall not attempt to give all the angles, only certain important ones. I have seen some of the measurements referred to in textbooks; others I have not seen recorded in either textbooks or articles. In Bohler's book reference is made to certain angles, especially the salient angles of the os calcis.

### THE METHOD

Figure 1 shows two rulers, one of which is useful in drawing lines and measuring angles. A similar one should be at hand whenever reports are to be written.

Figure 2 shows the way these lines are drawn to get these angles.

*Ankle and Foot.*—Perhaps there is no more important place for insistence on correct anatomic alignment than in the ankle and foot. These bones have the hard work to do. You are all aware of the disability which occurs if there remains a valgus or a posterior displacement of the os talus or a widening of the tibial mortise.

A diagrammatic representation of a normal ankle with a Pott's fracture is shown in Figure 2. Figure 3 shows the same type fracture before and after reduction. You will notice a line drawn through the central axis of the tibia. Record in centimeters the distance the center of the talus is from this axial line. Also record the angle of valgus or varus.

In lateral views of the ankle the posterior displacement of the talus should be recorded in centimeters from the axial line, or by an angle from the axial line. In fractures above the ankle the mortise may be

Fig. 3.

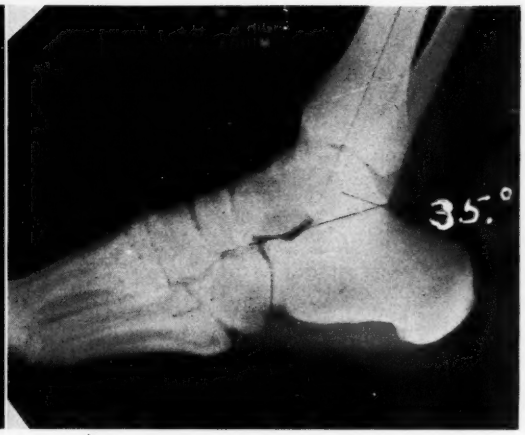


Fig. 4.

Fig. 3. On the right is an old Pott's fracture before attempted reduction, with 20-degree valgus. On the left is the reduction, with 12-degree valgus.

Fig. 4. Lateral view of a normal ankle. Draw one line from the upper anterior border to the posterior border of the talus facet. Draw another line from this latter point to the upper border of the tuberosity. The angle here is 32 degrees.

intact, in which case it is important to record how far the joint is from the perpendicular to the central axis of the proximal tibia. The line drawn parallel to the upper border of the mortise of the joint should be at right-angles to the central axis. Again in Figure 3 may be seen an old fracture, in which case it was impossible to reduce the fracture completely, but it was possible to bring the top of the talus to right-angles with the central axis. This is important in order to obtain even a fair functional result.

Figure 4 shows the lines that should be drawn on the os calcis to determine the salient angles and abnormal angles after certain types of fractures. In a lateral view of an ankle, the central axis of the tibia should fall in the middle of the os talus.

*Leg Injuries*.—In automobile injuries especially we have found it advisable to use long narrow films—7 × 17. These are much easier to use than 14 × 17 films divided. Either the knee joint or the ankle joint will be included in these films, sometimes both. They are also advisable for use in suspected fractures of the femur. We have all seen cases in which one fracture has been x-rayed while another higher up or lower down has gone unsuspected. This precaution will save worry and perhaps a law suit.

*Knee*.—As I looked at knee films from day to day, it occurred to me that most

Fig. 5. Lines are drawn through the axis of the anatomic neck of the femur and through the axis of the shaft. The angles here measure 125 and 127 degrees.

knee joints are slightly narrower medially than laterally. Accordingly I measured all the knees on the films in the hospital files which had no fractures into the joint. I found, in brief, that 70 per cent had from 0.1 to 0.3 cm. narrowing of the medial joint space. Our most common reading was 0.5 cm. medially and 0.6 cm. laterally. These measurements were taken in the middle of the medial and lateral joint spaces. Twenty per cent measured the same on both sides and 10 per cent were narrower laterally than medially. The normal young adult should have both sides of the joint equal. Older individuals, of which more films are found in hospital files, have a large proportion of narrower joint spaces medially.

*Hip.*—We like to make stereoscopic views including the good hip as well as the injured one. We also make the lateral view through the neck of the femur on the injured side. For the anteroposterior views, the legs should be immobilized in internal rotation. The lower medial angle has been recorded by us, and we find an average measurement of 135 degrees. In addition to giving this angle, one should record in centimeters the upper displacement of the shaft, and so forth.

*Long Bones.*—One should draw the central axial lines in each fragment and record in degrees their deviations from one another. If these lines are parallel, you should state their separation from one another.

*Spines.*—The normal curve of the spine is not fixed. In fractures of the vertebral bodies it is well to draw lines and record the angle of deviation from each vertebra so that the degree of improvement after reduction can be noted.

*Shoulder.*—It is somewhat difficult to measure the normal angle of the neck with the shaft of the humerus because there are often variations in the direction of the central x-ray beam. Also rotation has an influence on this angle. We have our films made with the arm externally rotated and with the hand in supination. The average lower medial angle is 140 degrees.

*Elbow.*—Figure 6 shows the lines drawn for the lateral angle and for the anterior angle in an adult. In children, one of the most common fractures is a supracondylar fracture of the humerus. In this the distal fragments are angled posteriorly. The normal measurements are taken by drawing the axial line in the distal third of the humerus. A line parallel to this which will just touch the anterior cortex of the humerus above the condyles is then drawn.

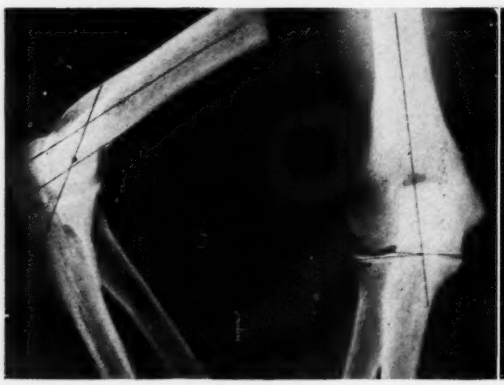

Fig. 6.

Fig. 7.

Fig. 6. Anteroposterior and lateral views. In the lateral view note the axial line in the center of the humerus and the anterior cortical line parallel to it. The anterior angle here is 40 degrees.

Fig. 7. Supracondylar fracture in a child. The center of the epiphysis is posterior to the anterior cortical line and the anterior angle is reduced to 25 degrees.

A point in the center of the condyles, as shown in the lateral view, is then connected by a line drawn through the middle of the neck of the condyles. This gives the normal anterior angle. The center of the condyle in children should fall anterior to the anterior axis; in adults it falls posteriorly.

*Wrist.*—Colles' fractures are very common in adults. Almost every doctor in general practice tries to reduce these fractures and it is probably right that he should do so, but I do think he often does it rather poorly. We, as roentgenologists, can show him by measurement how far he has come from the normal. We can insist that he has the articulating surface of the radius at least at right-angles to the central axis of the shaft, or, better yet, to the normal 5-degree ventral inclination.

Under local injection into the fracture the doctor can often reduce the fracture in his office. This saves hospital expense and much time and effort. Relaxation of the muscles is often more complete under local anesthesia than under gas.

*Conclusion.*—I have attempted to give certain important angles that will aid in determining whether or not the fracture is completely reduced. It is hoped that some of the common normal angles will be clearly remembered when these fractures are reported. I believe roentgenologists can assist the surgeon more if they can indicate the amount of deviation from the normal in the way I have outlined. Our accuracy will make for greater accuracy on the part of the surgeon.

Acknowledgment is made of helpful encouragement and suggestion from R. D. Joldersma, M.D.

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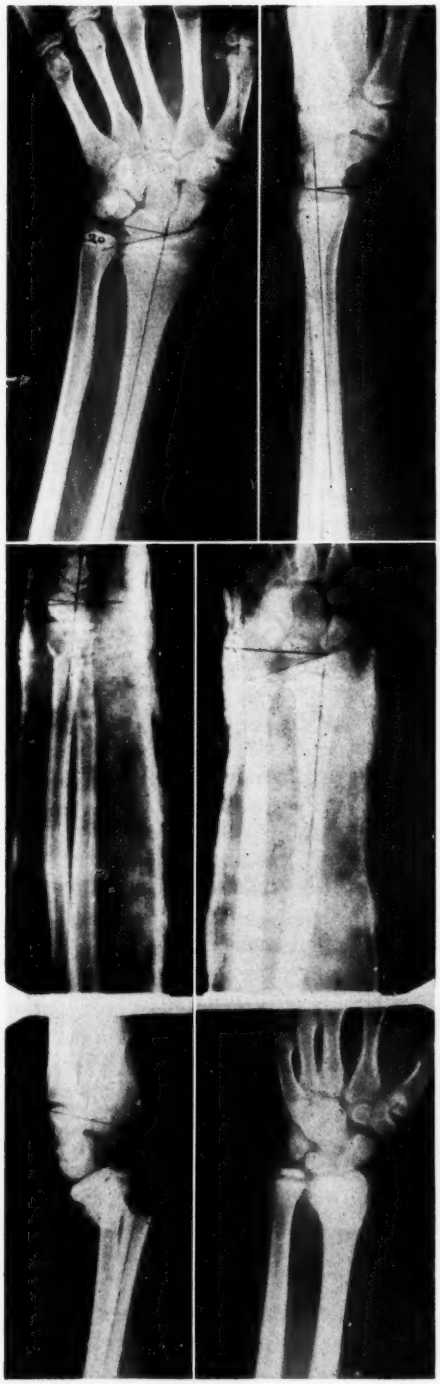

Fig. 8. Anteroposterior and lateral views of a normal wrist. In the anteroposterior view the normal medial slope of the articulating surface of the radius is shown. In the lateral view the normal three- to five-degree anterior slope of this articular surface is shown. (*Upper right.*)

Fig. 9. Anteroposterior and lateral views before and after reduction. This is a satisfactory reduction done in the office under local anesthesia.

# FURTHER STUDIES ON THE EFFECTS OF IRRADIATION ON PROLIFERATION AND METABOLIC PROCESSES OF NORMAL AND MALIGNANT TISSUES[1]

## IV. EFFECTS PRODUCED BY DIFFERENT DOSAGE RATES OF X-RAY RADIATION ON THE PROLIFERATION OF VARIOUS TISSUES GROWN *IN VITRO*

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THE time-intensity factor related to the effectiveness of irradiation upon living processes remains to-day an unsettled problem among the investigators in this specialized field. The question as to whether high dosage rates for a short time or low dosage rates for a long period of exposure produce more marked effects of radiation has not yet been definitely answered. The present series of experiments was undertaken in an attempt to throw some light upon this question. Before presenting the results obtained from these experiments, reference will be made to our previous investigation (1).

The determination of the lethal and sublethal doses produced by different types of radiation for various tissues grown *in vitro* was chosen as a basis for that investigation. The following technic and criteria were used: Freshly excised tissue fragments embedded in a nutritive medium on a No. 1 coverslip and covered with a mica sheet were inverted over a hollow ground slide, sealed with paraffin wax, and irradiated. The irradiated, as well as the control cultures, were incubated at 37.5° C. The amount of irradiation which inhibited the proliferation of an explant during 48 to 72 hours of incubation was termed the lethal dose; the highest amount of radiation which just permitted a slight proliferation of the explant to take place during 48 to 72 hours of incubation was arbitrarily termed the sublethal dose. In experiments since performed, it was observed that those explants which did not show any proliferation when incubated in the irradiated medium grew quite normally, or to a certain extent, when transferred to a fresh medium.

In the present experiments a different procedure was used. Freshly excised tissue fragments ranging from two to five milligrams were placed in a very thin layer of the usual nutritive medium, just enough to make the tissue fragments adhere to the No. 1 coverslip; they were covered with a mica sheet, inverted over a hollow ground slide, sealed with paraffin wax, and irradiated. The tissue fragments, after being removed from the nutritive medium immediately following irradiation, were washed in Tyrode solution for about five to ten minutes; the larger fragments of about five milligrams were then cut into smaller portions of about one milligram and were placed in a freshly prepared medium. Cultures were made and incubated in the usual way. Control cultures were made, using the same procedure, except that they were not irradiated.

The results obtained from these experiments were not as uniform as in the previous ones in which the explants were left in the irradiated medium. The viability of the individual explants decreased with the increase of the time of exposure and dose of irradiation administered. The number of irradiated explants, both the proliferating and non-proliferating, was counted and compared with those of the controls. The percentage of the non-proliferating explants was used as a criterion for the effectiveness of the dose of irradiation applied.

The use of small fragments of freshly excised tissues from the animal body

[1] Presented at the Third International Cancer Congress, in Atlantic City, N. J., September, 1939.

seemed to be more appropriate for this study than cell colonies grown *in vitro*, since the therapeutic radiations are also applied to the tissues as a whole and not to cells grown *in vitro*. The objections made by some investigators, that cells cultivated *in vitro* for some time do not possess the same qualities as body cells, can be overcome when freshly excised tissues are used.

## MATERIAL AND EXPERIMENTAL PROCEDURE

Tissues used in these experiments were: kidneys and spleens of one- to two-day-old rats, Mouse Sarcoma 180 of eight- to ten-day growing tumors in the animal body, and eight-day-old chick embryo hearts. The nutritive medium used for chick embryo hearts consisted of an extract made from eight-day-old chick embryos in Tyrode's solution and fowl plasma in the proportion of 1 : 1. For the cultivation of mammalian tissues, such as the rat kidneys, spleen, and Mouse Sarcoma 180, three parts of human blood serum were added to the medium mentioned above. A drop of the medium was spread on a No. 1 coverslip and the cultures were made according to the procedure already described. The thickness of the No. 1 coverslip plus the mica sheet was 0.1 mm. This was added to the distance from the target to the tissue for the calculation of the final dose administered. The tissues were irradiated at room temperature of about 22 to 24° C.

Three different dosage rates of x-rays (234 r/min., 936 r/min., and 10,000 r/min.) were used in these experiments. The source of x-rays for both dosage rates of the same quality (936 r/min. and 234 r/min.) was a pulsating potential, two-valve generator with an oil-cooled Westinghouse heavy glass x-ray tube, the physical factors being 200 kv., 20 ma., 0.5 mm. Cu, 1 mm. Al filter, and a half value layer of 0.85 mm. copper. Using a tissue–target distance of 25.0 cm. or 12.5 cm., the average dosage rate was 234 r/min. and 936 r/min., respectively, without back-scattering. The source of x-rays producing a dosage rate of 10,000 r/min. was a constant potential, single valve, forced air-cooled tube.[2] The tube is of a special construction to permit the very short target distance of 18 mm. and has a low inherent filtration of about 0.2 mm. of aluminum. The physical factors were 44 kv., 2 ma., 0.2 mm. Al, 18 mm. target distance, and half value layer of 0.28 mm. Al. Under these conditions 10,000 r/min. was the average dosage rate measured in air without back-scattering. The radiation took place with the x-ray tube and mica cover sheet in contact, as demonstrated in Figure *A*, which made the actual tissue–target distance equal to 18.1 mm. Taking into consideration the thickness of 0.1 mm. of the No 1 coverslip plus mica, the actual radiation received by the tissue was approximately 3 per cent less than the dose indicated, due to both increased distance and absorption by the coverglass.

Explants of kidneys and spleens from one- to two-day-old rats as well as explants of eight-day-old embryo chick heart always produce abundant growth of new cells. The evaluation of the growth of the irradiated explants was based upon a comparison with control cultures of which 100 per cent (in every instance) produced good growth.

In the experiments with Sarcoma 180, however, a different evaluation of the results had to be applied. Although this type of tumor produces 100 per cent takes when inoculated into a susceptible strain of mice, it does not yield 100 per cent positive growth when cultivated *in vitro*. Only a variable number of explants, in most instances, produce growth. Hence the percentages of growing explants of the control cultures and the irradiated cultures were compared, evaluating the effectiveness of the dose of x-rays applied.

## EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT KIDNEYS, USING A DOSAGE RATE OF 936 r/MIN.

Freshly excised tissue explants of one- to two-day-old rat kidneys were irradiated

[2] I wish to express my thanks to the Philips Metalix Corporation for their courtesy in permitting me to use the machine producing 10,000 r per minute for these experiments.

by using the technic previously described. Cultures were made and observed during 48 to 72 hours of incubation following irradiation. The results obtained with different doses of x-radiation are recorded in Table I. (Since the control cultures always yielded 100 per cent positive growth, it was regarded unnecessary to record them in the tables.) An area of new growing cells, both epithelia and fibroblasts, occurred around the explants during 24 hours of incubation following radiation with 40,000 and 50,000 r. The newgrowth increased in size during the next 24 hours of incubation. The size of the newgrowth of the irradiated explants did not apparently differ from that of the control cultures. The new cells, both epithelia and fibroblasts, appeared normal. The many mitotic figures present in the irradiated cultures served as evidence that the newgrowth consisted of new actively growing cells and not of emigrating cells.

A marked effect of irradiation could be noticed with doses starting from 60,000 r. An increase of the dose applied resulted in a corresponding decrease in the percentage of growing explants. For example, when a dose of 60,000 r was applied, 78.6 per cent of the irradiated explants produced newgrowth; when a dose of 70,000 r was applied, 47.1 per cent of the irradiated explants produced newgrowth. When the applied dose was 90,000 r, growth occurred in 8.33 per cent of the irradiated explants. In some cultures containing explants previously irradiated with 95,000 r, scattered cells in the field could be observed which probably emigrated from the explants, but there was no homogeneous growth and no mitotic figures were present. No newgrowth or scattered cells could be observed in the cultures containing explants which had been irradiated with 100,000 r.

It should be emphasized that irradiated explants which produced even a very small number of new growing cells were classified as positive in regard to the percentage of growing explants, although the growth produced by the control cultures was of much larger size.

It is to be noted that the experiments with 70,000 and 90,000 r (see Experiments 4 and 5, Table I) were carried out at the same time using tissue from the same kidneys. The experiment with 90,000 r, within the critical dosage, was repeated with a larger number of explants. The percentage of growing explants of both experiments differs by 3 per cent (see Experi-

TABLE I.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT KIDNEY, USING A DOSAGE RATE OF 936 r/MIN.

| No. of Experiment | Time of Radiation in Min. | Dose in r | No. of Irradiated Explants | Percentage of Growing Explants | Remarks |
|---|---|---|---|---|---|
| 1 | 42¾ | 40,000 | 12 | 100 | No marked difference could be observed between the newgrowth of the irradiated and control cultures |
| 2 | 53½ | 50,000 | 10 | 100 | |
| 3 | 64¼ | 60,000 | 14 | 78.6 | |
| 4 | 75 | 70,000 | 17 | 47.1 | The newgrowth of the irradiated explants was much smaller and thinner than that of the controls. These two experiments were carried out at the same time with tissues from the same kidneys |
| 5 | 96¾ | 90,000 | 12 | 8.33 | |
| 6 | 96¾ | 90,000 | 18 | 11.1 | Only 3 per cent difference in growth occurred between Experiments 5 and 6. Experiments 6 and 7 were carried out at the same time with tissues of the same kidneys |
| 7 | 101½ | 95,000 | 18 | Only single cells | |
| 8 | 106½ | 100,000 | 14 | 00 | No growth at all occurred in the irradiated cultures, while the control cultures produced excellent growth |

ments 5 and 6), which indicates that the results can be reproduced in about 3 per cent under these conditions.

An analysis of the observations made from these experiments reveals that doses ranging from 90,000 to 95,000 r, using a dosage rate of 936 r/min., may be regarded as critical dosage levels preventing the proliferation of one- to two-day-old rat kidneys.

In addition to the effect of irradiation upon proliferation, the following observations were made within the critical doses of x-rays applied. A latent period of two to three days was noted before the occurrence of new cells. For example, explants irradiated with 50,000 r produced growth during 24 hours of incubation, but when irradiated with larger doses, for example, 70,000 to 80,000 r or more, growth did not occur before 48 to 72 hours of incubation, if at all. In such cases the newgrowth consisted of only a thin small growth of cells around the explant. These new cells had only a little heavily granulated protoplasm which was not as transparent as that of normal cells in the control cultures.

Another noteworthy phenomenon was observed within the critical dosage levels. An empty zone, surrounding the explants, could be seen in the fixed and stained cultures. This empty zone was present only in cultures where newgrowth occurred, while irradiated explants which did not produce newgrowth were not surrounded with an empty zone. The empty zones probably indicate the amount of the liquefied nutritive medium. Such empty zones around the explants are frequently observed in growing cultures of Sarcoma 180, not only of irradiated explants but also of controls.

It would be difficult to offer an explanation for this phenomenon. It may, however, be assumed that some changes are produced in the irradiated tissue which are responsible for the liquefaction of the nutritive medium in which this newgrowth takes place. It may also be assumed that the new cells produced by the explants previously irradiated with heavy doses of x-rays have a short lifetime and they disintegrate in the earlier stages or generations. (This point will be more thoroughly discussed later on.) In some of these empty spaces surrounding the explant, clumps consisting of several cells were observed; occasionally in the empty zone surrounding the explants stained nuclei predominated, while the protoplasm seemed to be shrunken, in some instances even dissolved, leaving only the nucleus. Figures 1, 2, and 3 demonstrate in part and serve as an example for the experiment with rat kidneys irradiated with x-rays using a dosage rate of 936 r/min.

### EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT KIDNEYS, USING A DOSAGE RATE OF 234 r/MIN.

The same kind of tissues using the same experimental procedure and the same physical factors as in the experiments with 936

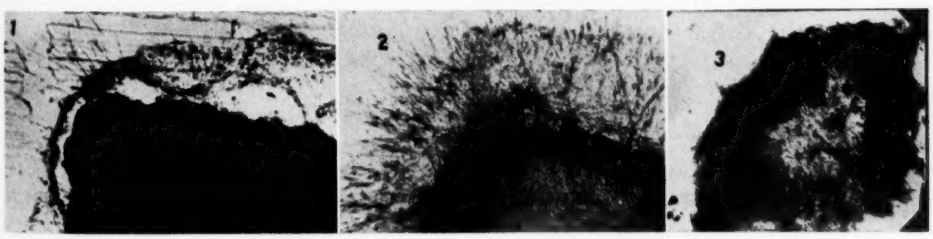


Fig. 1. A 72-hour growth *in vitro* of one-day-old rat kidney previously irradiated with 70,000 r during 75 minutes' exposure. Note the small growth of epithelia and fibroblasts and a zone of liquefaction, in which single cells, faintly stained, can still be seen.

Fig. 2. A 48-hour growth *in vitro* of one-day-old rat kidney. (Control for Fig. 1.) Note the dense growth of epithelial cells and thin growth of fibroblasts.

Fig. 3. An explant of one-day-old rat kidney irradiated with 100,000 r. No growth at all occurred during 72 hours' incubation.

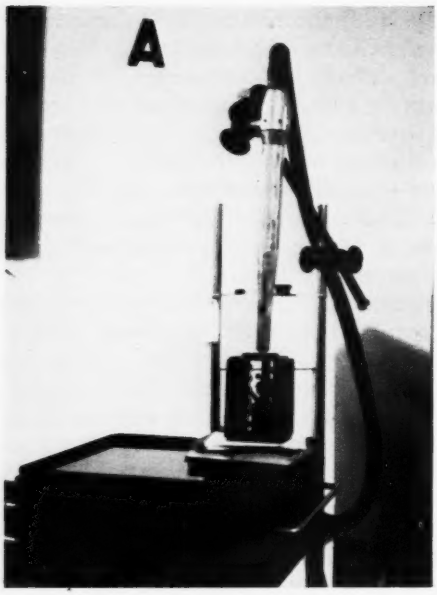


Fig. *A*. Shows position of x-ray tube producing 10,000 r/min. during irradiation of tissue explants.

r/min. were applied here, but with the exception that the tissue–target distance was increased from 12.5 to 25 cm., which decreased the dosage rate four times in accordance with the inverse square law.

In Table II are recorded a few results obtained from the effect of x-radiation upon the proliferation of one- to two-day-old rat kidneys by using a dosage rate of 234 r/min. Only the most striking observations made in this experiment will be discussed. A marked effect of radiation began to be noted with a dose of 50,000 r. In this experiment a reduction in the number of growing explants, as well as a decrease in size of the newgrowth produced by the irradiated explants, was noticed, when compared with those of control cultures. As can be seen in Table II, the doses ranging from 70,000 to 80,000 r permitted only a very small percentage of irradiated explants to produce a small growth of new cells. This growth occurred 48 to 72 hours after irradiation which indicates that there was a latent period of from two to three days. The destructive effects of irradiation in these experiments seemed to parallel the time of exposure rather than the dose of x-rays applied. The following analysis of the results obtained with both dosage rates (936 r/min. and 234 r/min.) will throw more light on this point.

By comparing the effects produced by the same dose of x-rays with the two different dosage rates, as recorded in Tables I and II, a decrease in percentage of the growing explants was noted with the increase of the time of exposure. For example, 100 per cent growing explants were observed after radiation with 50,000 r, given during 53 minutes and 20 seconds of exposure, while 85.7 per cent of growing explants were obtained with the same dose given during 213 minutes and 40 seconds of exposure. With a dose of 70,000 r given during 75 minutes exposure, using a dosage rate of 936 r/min., 47.1 per cent growing explants were observed, while 11.1 per cent of growing explants were obtained when the same dose of x-rays was applied with a time of exposure of 299 minutes using a dosage rate of 234 r/min. A dose of x-rays between 75,000 and 80,000 r applied during exposures of 320 and 342 minutes, respectively, using a dosage rate of 234 r/min., permitted only emigration of cells or a very small thin growth of a few of the irradiated explants. On the other hand, a dose of 95,000 r with an exposure of 101 minutes and 30 seconds using a dosage rate of 936 r/min. was required to produce similar effects.

The newgrowth, which occurred in some of the cultures which were irradiated with 75,000 r during 320 minutes using a dosage rate of 234 r/min., was small and thin; in some cultures only a few scattered cells could be seen. This newgrowth was observed on the third day after irradiation. The cells in these cultures, both fibroblasts and epithelial cells, looked shrunken with little and heavily granulated protoplasm, while explants irradiated with 70,000 r during 75 minutes' exposure, using a dosage rate of 936 r/min., gave 47.1 per cent good growth of epithelia and fibroblasts. Newgrowth had already occurred during 24 hours of incubation following radiation.

The graph (Fig. *B*) shows curves representing the main results recorded in Tables I and II. Although the curves do not record many intervening points, they, however, demonstrate clearly that a lower dosage rate requires less dosage for the same effect. Moreover, the drop in growth is much greater for a lower dosage rate for a given dose. A tentative explanation for these phenomena will be discussed later.

An analytic comparison of the percentage of growing explants, size of newgrowth, appearance of the new cells, and the duration of the latent period in experiments with 936 r/min. and 234 r/min. reveals that more damage is done to the tissue cells during a longer time of exposure using a lower dosage rate than with a high dosage rate and short time of exposure. Observations made from further experiments which will be discussed later support this view.

EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT KIDNEYS, USING A DOSAGE RATE OF 10,000 r/MIN.

The same type of tissue, *i.e.*, one- to two-day-old rat kidneys, and the same technical procedure were applied here as described in the previous experiments. The new type of x-ray apparatus, producing 10,000 r/min., has already been described. Only the observations made with effective doses of irradiation which are recorded in Table III will be discussed here.

Of explants irradiated with 90,000 r, 86.7 per cent produced growth during 24 hours of incubation following radiation. The size of the newgrowth and the appearance of the cells did not differ markedly from that of control cultures. The effect of irradiation first became apparent with a dose of 110,000 r. The explants which produced growth following irradiation with

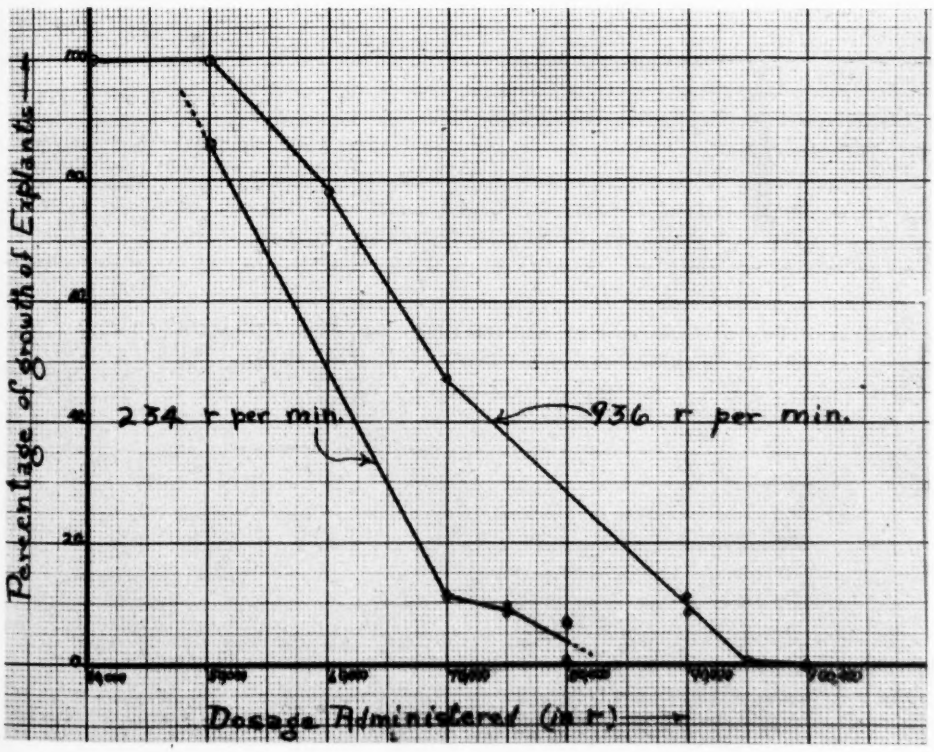


Fig. *B*. Observations from curves. It can be seen that a lower dosage rate requires less dosage for the same effect, and that the drop in growth is much greater for lower dosage rate than for higher dosage rate for a given dosage.

this dose had a latent period of 48 hours. The newgrowth was much smaller and thinner than that of the explants irradiated with a smaller dose, for example, with 90,000 r. A zone of liquefaction, as described in previous experiments, could also be observed in some of the irradiated cultures. These phenomena became still more pronounced when higher doses of x-rays were applied. For example, when explants were irradiated with 120,000 r, 33.3 per cent produced a small thin area of newgrowth, which occurred after 48 hours of incubation following radiation. A liquefaction of the medium produced by the newgrowth was observed in some of the cultures. When explants were irradiated with 130,000 or 140,000 r, growth of a few cells appeared in some of the cultures. If newgrowth appeared following the application of these doses of x-rays, it did not appear before the third day of incubation. The new cells did not have a healthy appearance. They were shrunken, containing little and heavily granulated protoplasm. In the fixed and stained cultures, a large

TABLE II.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT KIDNEY, USING A DOSAGE RATE OF 234 r/MIN.

| No. of Experiment | Time of Radiation in Min. | Dose in r | No. of Irradiated Explants | Percentage of Growing Explants | Remarks |
|---|---|---|---|---|---|
| 1 | 213⅔ | 50,000 | 14 | 85.7 | The area of newgrowth was smaller and thinner than that of the controls |
| 2 | 299 | 70,000 | 18 | 11.1 | Only a very thin and small growth occurred around the explants after 48 hours of incubation. A zone of liquefaction was observed |
| 3 | 320 | 75,000 | 24 | 8.33 | These two experiments were carried out at the same time using tissues from the same kidneys |
| 4 | 342 | 80,000 | 15 | 6.67 | |
| 5 | 320 | 75,000 | 31 | 9.68 | These two experiments are a repetition of Experiments 3 and 4. Similar results were obtained. In Experiment 6 only few scattered cells were observed in some of the cultures |
| 6 | 342 | 80,000 | 26 | Only single cells | |

TABLE III.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT KIDNEY, USING A DOSAGE RATE OF 10,000 r/MIN.

| No. of Experiment | Time of Radiation in Min. | Dose[1] in r | No. of Irradiated Explants | Percentage of Growing Explants | Remarks |
|---|---|---|---|---|---|
| 1 | 9 | 90,000 | 15 | 86.7 | The newgrowth was smaller than that of the controls |
| 2 | 10 | 100,000 | 17 | 82.4 | |
| 3 | 11 | 110,000 | 14 | 57.1 | The newgrowth was much smaller than that of the explants irradiated with 90,000 r |
| 4 | 12 | 120,000 | 18 | 33.3 | Among the growing explants, only a very small growth was observed, which occurred 48 hours after irradiation. Liquefaction around the growing explants occurred |
| 5 | 13 | 130,000 | 18 | 11.1 | |
| 6 | 14 | 140,000 | 15 | Only a few cells | Only single scattered cells could be observed in some of the cultures |
| 7 | 15 | 150,000 | 14 | 00 | |

[1] The actual dose received by the tissue is about 3 per cent less than the indicated dose.

zone of liquefaction around the explant was observed, in which cells had clumped together. In some of these empty spaces only the nucleus of the cells remained, without any protoplasm being evident. As may be remembered, the phenomenon of liquefied areas around the explants also occurred in the experiments with 234 r/min. and 936 r/min., and persisted particularly within the critical dosage levels.

By comparing the results obtained with the two highest dosage rates applied in these experiments, *i.e.*, 10,000 r/min. and 936 r/min. and by not taking into consideration the qualities of x-rays, it can be noted that with a dose of 90,000 r given during a time of exposure of 96 minutes and 45 seconds, using a dosage rate of 936 r/min., 8.33 per cent of the irradiated explants produced a small growth of new cells, while with the same dose given during nine minutes of exposure, using a dosage rate of 10,000 r/min., 86.7 per cent of irradiated explants produced fairly good growth. With a dose of 100,000 r given during 106 minutes and 40 seconds of exposure, using a dosage rate of 936 r/min., no growth of new cells occurred in the cultures, while of explants irradiated with the same dose of 100,000 r given during 10 minutes of exposure, using a dosage rate of 10,000 r/min., 82.4 per cent produced growth of new cells. However, a dose of 120,000 r or 140,000 r given during 13 or 14 minutes of exposure, respectively, using a dosage rate of 10,000 r/min., either prevented entirely the proliferation of explants of one- to two-day-old rat kidneys, or permitted only a very thin growth of new cells. Hence, the destructive effect here occurred more suddenly and in a narrower range of dosages applied than in the previous experiments with lower dosage rates.

The effects produced within the critical dosage levels of 130,000 and 140,000 r, using a dosage rate of 10,000 r/min., correspond to those obtained with a dose of 95,000 r using a dosage rate of 936 r/min. Consequently, the effect of x-rays upon the proliferation of tissue (in this case of rat kidneys), which can be produced with a dosage rate of 936 r/min. during a time of exposure of 101 minutes and 30 seconds, can be obtained during 13 minutes of exposure with a dosage rate of 10,000 r.

These observations were substantiated by other experiments with embryo chick heart, rat spleen, and Mouse Sarcoma 180, the results of which will be briefly discussed further on.

In repeated experiments within the critical doses of x-rays, the following observations were made: For example, in one experiment when explants were irradiated with 130,000 or with 140,000 r, one or two explants producing a very small growth of epithelia or fibroblasts could be found, while in another experiment using the same critical doses, no newgrowth at all could be observed. Among explants irradiated with 140,000 r, one producing a very small growth could be noted, while

Fig. 4. A 48-hour growth *in vitro* of one-day-old rat kidney following irradiation with 90,000 r given during nine minutes of exposure. Note a dense growth of epithelia and partial liquefaction of the medium.

Fig. 5. A 72-hour growth *in vitro* of one-day-old rat kidney previously irradiated with 110,000 r during 11 minutes' exposure using a dosage rate of 10,000 r/min. Note a small growth of epithelial cells and fibroblasts.

Fig. 6. Note a very small growth of a few epithelial cells and fibroblasts of one-day-old rat kidney previously irradiated with 130,000 r, using a dosage rate of 10,000 r/min., which occurred 72 hours after irradiation.

among explants irradiated with a lower dosage, such as 130,000 r, no growth at all occurred among the irradiated explants. In attempting to find an explanation for these phenomena a varied viability or different response of some of the cells to the high doses of x-rays may be assumed, or a delay in the reproductive ability may have occurred in some of the cells. Some cells survive or recover, others succumb. Figures 4, 5, and 6 serve as a partial demonstration of the experiments with 10,000 r/min. of x-rays.

### EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF CHICK EMBRYO HEART, USING A DOSAGE RATE OF 936 r/MIN.

Chick embryo heart usually produces 100 per cent positive growth of fibroblasts and serves, therefore, as an excellent index for experimental purposes. Chick hearts of eight-day-old embryos were used through all of the experiments. The technical procedure described in the preceding experiments with kidneys was applied here. Although a great number of experiments were carried out with various dosages of x-rays, only the results obtained with markedly effective doses, which are recorded in Table IV, will be discussed here. (It should be remembered that due to the fact that the control cultures always produced 100 per cent positive growth, it proved unnecessary to include them in the tables.)

Of explants irradiated with 90,000 r, 75 per cent produced newgrowth of fibroblasts. The newgrowth in some of the cultures did not apparently differ from that of the control cultures. Of 23 explants irradiated with 110,000 r, 11 produced growth, that is, 47.8 per cent. Among these, six cultures showed a very small and thin growth of fibroblasts, while five showed extensive growth, not differing markedly from that of the control cultures. Of 26 explants irradiated with 120,000 r, seven produced newgrowth, that is, 26.9 per cent: four of the explants produced extensive growth, and three a thin small growth of fibroblasts. Some of the explants were pulsating even 48 hours after irradiation. Of explants irradiated with 130,000 r, 25 per cent produced newgrowth. This growth, however, was thinner and smaller than that of the control cultures. The presence of many mitotic figures in the cultures served as evidence that the newgrowth consisted of new actively growing cells and not of cells which had emigrated from the explant. Many fat droplets were present, indicating early degeneration. Among 37 explants irradiated with 140,000 r, four produced very thin and small growths of fibroblasts, that is, 10.8 per cent. This growth occurred after 48 hours of

TABLE IV.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF CHICK EMBRYO HEART, USING A DOSAGE RATE OF 856 r/MIN. AND 936 r/MIN.

| No. of Experiment | Time of Radiation in Min. | Dose in r | No. of Irradiated Explants | Percentage of Growing Explants | Remarks |
|---|---|---|---|---|---|
| 1 | 105 | 90,000 | 16 | 75.0 | Among the growing explants some showed small, some extensive, growth of fibroblasts |
| 2 | 129 | 110,000 | 23 | 47.8 | Six explants produced small thin growth, five an extensive growth |
| 3 | 140 | 120,000 | 26 | 26.9 | The growing explants were pulsating 48 hours after irradiation |
| 4 | 139 | 130,000 | 24 | 25.0 | The growing explants produced very thin small growth. Fat droplets were present |
| 5 | 149½ | 140,000 | 37 | 10.8 | Only a very small growth of scattered cells occurred during 48 hours after irradiation |
| 6 | 160 | 150,000 | 28 | 3.57 | Only a few cells were observed in one of the cultures |

incubation following irradiation. Since a large zone of new cells was produced in each of the control cultures as early as 24 hours after incubation, it is evident that there was a latent period of 24 hours before newgrowth appeared in the irradiated explants. The new-growing cells appeared shrunken, with little heavily granulated protoplasm. Explants irradiated with 150,000 r produced either no growth or only a few scattered cells in some of the cultures. For example, among 28 explants only one showed a few growing cells. The experiment with 150,000 r was repeated three times and similar results were obtained each time. Consequently, the dose of 150,000 r, with a dosage rate of 936 r/min., may be regarded as a dose preventing proliferation of fibroblasts of eight-day-old chick embryo heart. Figures 7, 8, and 9 demonstrate, in part, the results of the experiments using an x-ray dosage rate of 936 r/min.

EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF CHICK EMBRYO HEART, USING A DOSAGE RATE OF 10,000 r/MIN.

The same material and experimental procedure were used here as for the preceding experiments with 936 r/min. The majority of experiments were carried out simultaneously, using tissues from the same eight-day-old chick embryo heart. Only the results obtained with effective doses of x-rays on the proliferation of explants, which are recorded in Table V, will be discussed.

With a dose of 100,000 r, 85.7 per cent of the irradiated explants produced newgrowth of fibroblasts. In some of the cultures the size of the newgrowth and appearance of the cells did not markedly differ from those of the control cultures. With higher doses, such as 120,000 and 150,000 r, the percentage of explants producing newgrowth of fibroblasts still remained within the same limits, *i.e.*, between 81 and 82 per cent. The newgrowth, however, was much thinner and smaller than that of the control cultures. Some explants produced only one or two layers of thin scattered cells. As previously mentioned, explants producing only a very thin and small growth of new cells were regarded as positive results. The presence of mitotic figures provided evidence that the newgrowth in the cultures consisted of actively growing cells. A dose of 200,000 r permitted only 25 per cent of explants to produce a newgrowth of fibroblasts which occurred after 48 hours of incubation. This newgrowth was very thin and small in size in comparison with that of the control cultures. A large empty zone, probably produced by liquefaction of the nutritive medium by the newgrowth, was present in the fixed and stained cultures. A dose of 225,000 r permitted 22.7 per cent of irradiated explants to produce growth, while a dose of 250,000 r permitted only 10 per cent among the irradiated explants to produce growth of new cells after 48 or 72 hours of incubation. It should be emphasized again that the growth which occurred

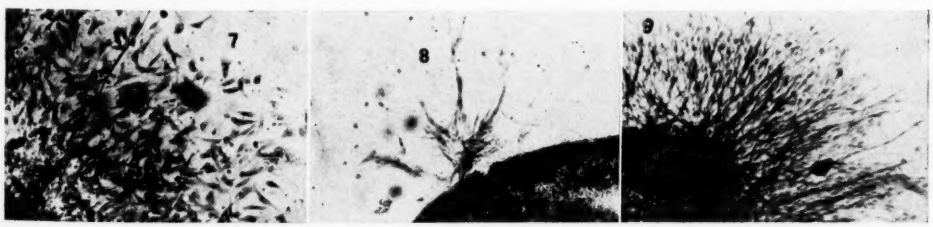


Fig. 7. A 48-hour growth *in vitro* of chick embryo heart previously irradiated with 130,000 r during 139 minutes' exposure using a dosage rate of 936 r/min. Note a thin, not homogeneous, growth of fibroblasts.
Fig. 8. A 72-hour growth *in vitro* of chick embryo heart previously irradiated with 150,000 r during 160 minutes of exposure using a dosage rate of 936 r/min. Note the growth of a few fibroblasts.
Fig. 9. A 48-hour growth *in vitro* of chick embryo heart. (Control for Figs. 7 and 8.) Note a dense abundant homogeneous growth of fibroblasts.

with these high doses was very thin. Some explants produced only a few cells, and these occurred after 48 or 72 hours of incubation. The results of these experiments show that a latent period of two to three days occurred within critical dosage levels of x-rays applied to the explants. A liquefaction around explants previously irradiated with high doses and still producing growth persisted in most of the cultures. Explants irradiated with 260,000 r did not produce any growth. In one of 60 cultures, however, a few thin cells around the explant occurred. This growth is demonstrated in Figure 10. Since no mitotic figures could be detected in this culture, it was difficult to ascertain whether this newgrowth consisted of actively growing cells or of cells which emigrated from the irradiated explants.

A comparison of the effects produced by x-rays (not taking into consideration their qualities) using two different dosage rates, 936 r/min. and 10,000 r/min., upon the proliferation of eight-day-old chick embryo hearts, reveals the following: Doses of x-rays within the range of from 90,000 to 130,000 r applied during 105 to 139 minutes of exposure, respectively, using a dosage rate of 936 r/min., reduced the percentage of growing explants from 75 to 25 per cent. A dose of 150,000 r permitted only a very small percentage of irradiated explants to produce growth of a few cells. However, doses in a similar range, *i.e.*, of 100,000 to 150,000 r, applied to the same type of tissue during a time of exposure ranging from 10 to 15 minutes, using a dosage rate of 10,000 r/min., still permitted 81.2 per cent of the irradiated explants to produce newgrowth.

This growth did not apparently differ from that of the control cultures. A marked and sudden drop in percentage of growing explants occurred, starting with a dose of 200,000 r, applied during an exposure of 20 minutes, using a dosage rate of 10,000 r/min., and terminated at a level ranging from 250,000 to 260,000 r. Consequently, the critical dosage levels of x-rays which exerted destructive effects upon the growth of chick embryo hearts were reached with 150,000 r during 160 minutes of exposure using a dosage rate of 936 r/min., while a dose of 260,000 r given during an exposure of 26 minutes using a dosage rate of 10,000 r/min. was required to produce similar effects. The phenomena,

TABLE V.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF CHICK EMBRYO HEART, USING A DOSAGE RATE OF 10,000 r/MIN.

| No. of Experiment | Time of Radiation in Min. | Dose[1] in r | No. of Irradiated Explants | Percentage of Growing Explants | Remarks |
|---|---|---|---|---|---|
| 1 | 10 | 100,000 | 14 | 85.7 | The newgrowth of the irradiated explants did not apparently differ from that of the controls |
| 2 | 12 | 120,000 | 22 | 81.8 | The newgrowths in some of the cultures were thin and small; in some, extensive |
| 3 | 15 | 150,000 | 16 | 81.2 | |
| 4 | 20 | 200,000 | 48 | 25.0 | The newgrowth was very thin and small. In some cultures only scattered single cells were present. Liquefaction around the explants occurred |
| 5 | 22½ | 225,000 | 22 | 22.7 | |
| 6 | 24 | 240,000 | 20 | 20.0 | The newgrowths in the growing cultures occurred 48 hours after irradiation and were thin and small |
| 7 | 25 | 250,000 | 20 | 10.0 | Only a very thin and small growth of fibroblasts occurred in the proliferating explants |
| 8 | 26 | 260,000 | 14 | Only a few cells | Single scattered cells were present in some of the cultures |

[1] The actual dose received by the tissue is about 3 per cent less than the indicated dose.

such as an increase in the latent period and liquefaction of the nutritive medium which occurred within the critical dosage levels of 130,000 and 150,000 r, using a dosage rate of 936 r/min., failed to occur within the same doses of x-rays using a dosage rate of 10,000 r/min., but appeared within the critical doses of 250,000 to 260,000 r.

Based on the foregoing observations, it may be safely concluded that the same dose of x-rays applied during a longer period of exposure produced more destructive effects upon the proliferation of tissues than the same dose applied during a shorter period. Moreover, the degree of the destructive effects is dependent not only upon the time of exposure but also upon the dosage rate. This point will be brought out more thoroughly in the general discussion.

### EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF RAT SPLEEN, USING DOSAGE RATES OF 936 r/MIN. AND 10,000 r/MIN.

The experiments with spleens were carried out, in most instances, simultaneously with that of the kidneys, from the same one- to two-day-old rats. Spleens, removed under strictly aseptic precautions, were cut into small fragments and irradiated. Cultures were made, using the same technical procedure as previously described. Only the most marked effects produced by x-rays upon the proliferation of spleen fragments, as recorded in Table VI, will be discussed here. Doses of 40,000 r applied during a time of exposure of 42 minutes and 45 seconds permitted, in one experiment, 64.3 per cent of the irradiated explants to produce newgrowth; in another, 75 per cent. Zones around the explants, consisting of round cells and fibroblasts, occurred during the first 24 hours of incubation after irradiation. These newgrowths increased in size during the following 24 hours of incubation. The new cells did not apparently differ from those of the control cultures. However, the areas of the newgrowth of the irradiated explants were much smaller and thinner than those of the control cultures. Sudden and drastic effects of irradiation upon the spleen were noted when doses above 40,000 r were applied. For example, of explants irradiated with 50,000 r during a time of exposure of 53 minutes and two seconds, only 3 per cent produced small areas of round cells and fibroblasts, which occurred 48 hours after irradiation. At the same time, all of the control cultures produced an abundant growth of round cells and also fibroblasts which had already appeared 24 hours after irradiation. Explants of spleens irradiated with 55,000 or 60,000 r either did not produce any, or a very small number of, round cells. A small number of fibroblasts, however, were present in either case.

Analysis of the results reveals that the same dose of x-rays at the identical dosage rate produced more striking and rapid effects upon the proliferation of spleen explants than upon the proliferation of kidney explants from the same rat. For example, a dose of 60,000 r using a dosage rate of 936 r/min. prevented the proliferation of explants from the spleen, while the

TABLE VI.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION *in vitro* OF ONE-DAY-OLD RAT SPLEEN, USING A DOSAGE RATE OF 936 r/MIN.

| No. of Experiment | Time of Exposure in Min. | Dose in r | Percentage of Proliferating Explants | Remarks |
|---|---|---|---|---|
| 1 | $42^{3}/_{4}$ | 40,000 | 64.3 | Growth of round cells and fibroblasts occurred around the irradiated explants. This growth was smaller and thinner than that of the control cultures |
| 2 | $42^{3}/_{4}$ | 40,000 | 75.0 | |
| 3 | $53^{1}/_{30}$ | 50,000 | 30.0 | Only a very small growth of round cells and fibroblasts occurred during 48 hours' incubation |
| 4 | $64^{1}/_{4}$ | 60,000 | .. | Only a small growth of fibroblasts occurred in some of the cultures, but no round cells |

same dose permitted 78.6 per cent of the irradiated explants of kidneys to produce a fairly good growth of epithelia and fibroblasts.

From the experiments performed with rat spleen irradiated with x-rays at a dosage rate of 10,000 r/min., only one, as an example, will be mentioned here. Explants irradiated with 70,000 r during an exposure of seven min. produced dense zones of round cells around the explants during the first 24 hours after irradiation. The newgrowth increased in size during the following days of incubation. It should be remembered at this point that a dose of 70,000 r applied during an exposure of 75 minutes, using a dosage rate of 936 r/min., prevented the proliferation of explants of the same type of tissue, that is, rat spleen. These results again substantiate the evidence that the time of exposure, not only the dose, is an important factor in radiation effects.

Since the purpose of the present study was to determine the dose of x-rays which would prevent the proliferation of the tissue explant as a whole, no particular attention will be given here either to the type of cells which appeared in the cultures or to the intracellular changes produced by a given dose of x-rays. A detailed report of the latter characteristics, with more data of the experiments performed with rat spleens, will be given subsequently. It should be emphasized that since no mitotic figures could be observed in the irradiated as well as the control cultures of the spleen, it is difficult to ascertain whether the newgrowth in the cultures consisted of actively growing cells or cells which emigrated from the spleen explants. Figures 11, 12, and 13 demonstrate in part the results obtained from the experiments with rat spleen.

### EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF MOUSE SARCOMA 180, USING A DOSAGE RATE OF 936 r/MIN.

Fragments from eight- to ten-day-old tumors weighing about five milligrams were irradiated and cultures made by using the same procedure described in the previous experiments. An area of newgrowth consisting of macrophages, leukocytes, lymphocytes, and sarcoma cells is usually produced during 24 hours of incubation, which increases in size during the following days of incubation. Since the purpose of the present study was to detect the dose which would prevent the proliferation of the explant as a whole, no particular attention will be given here to the specific effect of irradiation upon the individual cells. Only a few results obtained with effective doses of x-ray, which are recorded in Table VII, will be discussed. With a dose of 30,000 r, 25 per cent of the irradiated explants produced newgrowth, while among the control cultures, 33.3 per cent produced newgrowth. Consequently, the failure of 8.3 per cent of the irradiated explants to produce newgrowth may be attributed to

TABLE VII.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION *in vitro* OF SARCOMA 180, USING A DOSAGE RATE OF 936 r/MIN.

| No. of Experiment | Time of Exposure in Min. | Dose in r | Percentage of Proliferating Irradiated Explants | Percentage of Proliferating Control Explants | Difference in Percentages | Remarks |
|---|---|---|---|---|---|---|
| 1 | 32.0 | 30,000 | 25.0 | 33.3 | 8.3 | No apparent difference between the irradiated and control cultures could be noticed |
| 2 | 42½ | 40,000 | 13.5 | 46.6 | 33.1 | |
| 3 | 53⅓ | 50,000 | 10.0 | 50.0 | 40.0 | The newgrowth of the irradiated explants was smaller than that of the controls |
| 4 | 64⅙ | 60,000 | 8.33 | 47.1 | 38.77 | Only small growth occurred in two of 24 irradiated explants |

the effect of the x-ray dose applied. A dose of 40,000 r permitted 13.5 per cent of the irradiated explants to produce newgrowth, while 46.6 per cent of the control cultures produced newgrowth. The difference of 33.1 per cent may also be regarded as the effect produced by irradiation. The failure of 40 per cent of the explants previously irradiated with 50,000 r (Experiment 3, Table VII) to produce a growth of new cells, can also be regarded as the result of the effects of irradiation.

With doses above 50,000 r in some cultures, a few of the irradiated explants produced newgrowth, in others, none at all. For example, among 24 explants irradiated with 60,000 r, 8.33 per cent, *i.e.*, two explants, produced a small growth of new cells, while of 17 control explants, eight produced newgrowth, *i.e.*, 47.1 per cent. The failure of 38.77 per cent of the irradiated explants to produce growth was possibly due to the effect of irradiation. Explants of Sarcoma 180 irradiated with doses above 60,000 r, for example, 70,000 to 80,000 r, failed to produce any newgrowth in experiments repeated several times, while a certain number of control cultures yielded fairly good growth in each experiment. Consequently, the dose of 60,000 r at a dosage rate of 936 r/min. applied during 64 minutes and 15 seconds exposure may be regarded as the dose which still permits a very small percentage of irradiated explants to produce slight growth. A dose above 60,000 r is the one which prevents proliferation of Sarcoma 180.

In the course of experiments with Sarcoma 180, the following observations were made: When the control cultures did not yield abundant newgrowth, the effect of irradiation seemed to be more striking and could be reached with a lower dose. For example, in repeated experiments with high doses of x-rays, as with 50,000 or 60,000 r in one experiment, no growth was noted among the irradiated explants, while in another, a certain number of irradiated explants produced a few cells. It is, therefore, important to note that in experiments in which the control explants do not yield 100 per cent positive growth, a large number of explants should be used for each experiment.

By comparing the results obtained with the same dosage rate of x-rays under the same conditions for two different types of tissues, *i.e.*, spleen from one- to two-day-old rats and Sarcoma 180, it can be noted that similar effects were produced by approximately the same doses of x-radiation. A dose of 60,000 r applied to both types of tissues during 64 minutes and 15 seconds permitted, in some instances, a small growth of new cells, and, in other instances, none at all. Accordingly, this dose of x-rays under the same conditions may be regarded as the minimum dose preventing proliferation *in vitro* for both types of tissues, *i.e.*, rat spleen and Sarcoma 180.

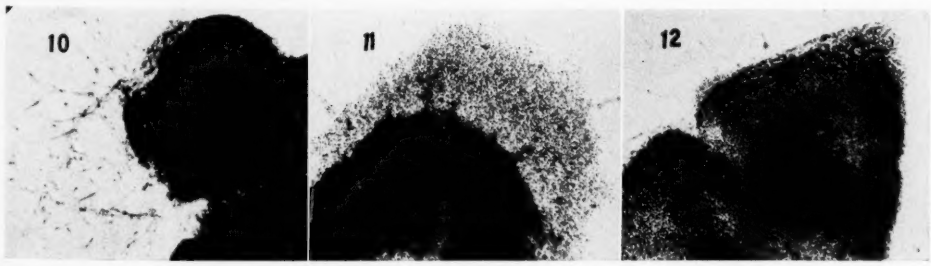


Fig. 10. A 72-hour growth *in vitro* of chick embryo heart following irradiation with 260,000 r given during 26 minutes' exposure using a dosage rate of 10,000 r/min. Note single scattered cells in the field.
Fig. 11. A 48-hour growth *in vitro* of two-day-old rat spleen previously irradiated with 50,000 r during 53 minutes and two seconds of exposure. Note a zone of round cells.
Fig. 12. An explant of two-day-old rat spleen irradiated with 70,000 r during 75 minutes' exposure using a dosage rate of 936 r/min. No newgrowth of round cells. Only a few fibroblasts can be noted.

EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION OF MOUSE SARCOMA 180, USING A DOSAGE RATE OF 10,000 r/MIN.

Experiments were carried out with Sarcoma 180 irradiated with x-rays at a dosage rate of 10,000 r/min. A major part of these experiments was performed simultaneously with those experiments in which a dosage rate of 936 r/min. was applied. Only the results recorded in Table VII will be discussed here. With doses of 50,000 and 80,000 r applied during five and eight minutes, respectively, 50 per cent of the irradiated explants coincidentally produced newgrowth in both experiments, while of the control explants, from 66 to 77.7 per cent produced newgrowth. A dose of 85,000 r permitted 33.3 per cent of the irradiated explants to produce newgrowth, while among the control explants 66.7 per cent produced newgrowth. Several experiments were repeated with higher doses of x-rays, for instance, with 90,000, 95,000, and 100,000 r. In one experiment with 90,000 r, only one out of 27 explants produced a very small growth of new cells. Comparing the results obtained with Sarcoma 180 irradiated with x-rays, using two different dosage rates, but not taking into consideration their quality, it can be noted that the minimum dose which still permitted slight proliferation of Sarcoma 180 was reached during 64 minutes and 15 seconds of exposure at a dosage rate of 936 r/min., while approximately the same effect was produced with an exposure of eight minutes and 30 seconds, using a dosage rate of 10,000 r/min. Figures 15, 16, 17, and 18 demonstrate the results of this experiment.

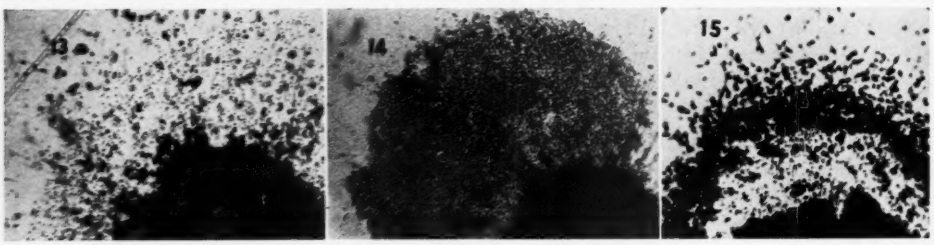


Fig. 13. A 48-hour growth *in vitro* of two-day-old rat spleen previously irradiated with 70,000 r during seven minutes' exposure using a dosage rate of 10,000 r/min. Note growth of round cells and of fibroblasts.

Fig. 14. A 48-hour growth *in vitro* of two-day-old rat spleen. (Control for Figs. 11, 12, and 13.) Note abundant growth of cells.

Fig. 15. A 48-hour growth *in vitro* of Sarcoma 180 previously irradiated with 40,000 r during 42 minutes and 30 seconds' exposure using a dosage rate of 936 r/min. Note a dense growth of various cells and liquefaction around the explant.

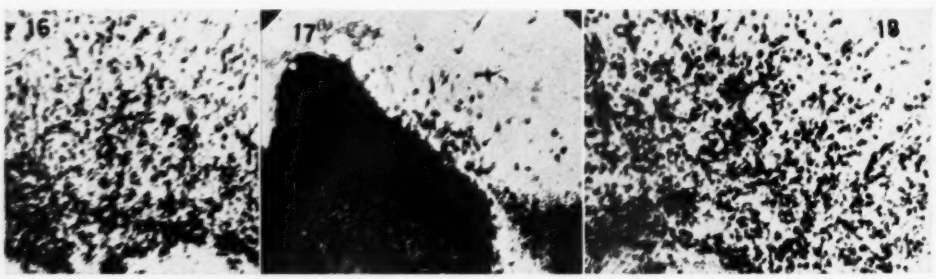


Fig. 16. A 48-hour growth *in vitro* of Sarcoma 180 previously irradiated with 50,000 r during five minutes' exposure using a dosage rate of 10,000 r/min. Note a large amount of cells and a zone of liquefaction.

Fig. 17. A 72-hour growth *in vitro* of Sarcoma 180 previously irradiated with 90,000 r during nine minutes' exposure using a dosage rate of 10,000 r/min. Note a very small growth of new cells.

Fig. 18. A 48-hour growth *in vitro* of Sarcoma 180. (Control for Figs. 15 to 18.) Note the abundant growth of new cells.

## SUMMARY AND INTERPRETATIONS OF THE RESULTS

A concise review of the results of these experiments is given in Table IX. This table contains the critical dosage levels of x-rays using different dosage rates for various tissues grown *in vitro*. As can be noted, similar effects on the proliferation of the same type of tissues, *i.e.*, of one- to two-day-old rat kidneys, were produced with dosages in the range of 90,000 to 95,000 r during a time of exposure of 96 to 101 minutes, respectively, with dosages between 75,000 to 80,000 r during a time of exposure of 320 to 342 minutes, respectively, and with dosages between 130,000 and 140,000 r during a time of exposure of 13 to 14 minutes, respectively. Analyzing these observations it can be noted that the effects of irradiation depend upon the dosage rate and time of exposure. This view is supported by the results obtained from experiments with chick embryo heart. Doses between 140,000 and 150,000 r applied during 150 to 160 minutes of exposure, using a dosage rate of 936 r/min., either permitted a very small growth of a few cells or inhibited entirely the proliferation of the irradiated explants. Similar effects were produced by dosages within the range of 250,000 to 260,000 r, during the time of exposure of 25 to 26 minutes, respectively, using a dosage rate of 10,000 r/min. (It should be recalled that the quality of x-rays using a dosage rate of 10,000 r/min. differs from those of the other dosage rates due to different filtrations.)

Further, a decrease in percentage of the irradiated explants with the increase of the time of exposure, using the same dose, was noted. The decrease in percentage of irradiated explants seems to bear a relation to the rate of exposure for a given dose, which is not, however, a direct proportion. This was noticed particularly for the lower dosages. Nevertheless, in the range of critical dosages a drastic decrease in the percentages of irradiated explants as well as in the size of newgrowth was noticed, corresponding, roughly, to the dosage rate. Thus, of explants irradiated with 50,000 r during a time of exposure of 53 minutes and 20 seconds, 100 per cent produced good growth, while the same dose applied during 213 minutes and 40 seconds permitted 85.7 per cent of irradiated explants to produce newgrowth. Of explants irradiated with 70,000 r during 75 minutes of exposure (using a dosage rate of 936 r/min.), 47.1 per cent produced newgrowth of epithelia and fibroblasts during 24 hours of incubation, while the same dose applied during 299 minutes (using a dosage rate of 234 r/min.) permitted only 11.1 per cent of the irradiated explants to produce a very small growth of new cells during 48 to 72 hours of incubation. It can also

TABLE VIII.—EFFECTS PRODUCED BY X-RAYS UPON THE PROLIFERATION *in vitro* OF SARCOMA 180, USING A DOSAGE RATE OF 10,000 r/MIN.

| No. of Experiment | Time of Exposure in Min. | Dose in r | Percentage of Proliferating Irradiated Explants | Percentage of Proliferating Control Explants | Difference in Percentages | Remarks |
|---|---|---|---|---|---|---|
| 1 | 5.0 | 50,000 | 50.0 | 66.0 | 16.0 | No apparent difference between the irradiated and control cultures could be noticed |
| 2 | 8.0 | 80,000 | 50.0 | 77.7 | 27.7 | |
| 3 | 8½ | 85,000 | 33.3 | 66.7 | 33.4 | A small growth occurred in the irradiated cultures while extensive growth occurred in the controls |
| 4 | 9.0 | 90,000 | .. | 38.7 | .. | Only one out of 27 irradiated explants produced small growth of new cells |

be noticed from these experiments that there was an increase in the latent period, *i.e.*, the lapse of time between the incubation of the explants and the appearance of new-growth within the increase of the time of exposure (using the same dose of filtered x-rays).

The analysis of the results recorded in Table IX reveals also a selective action of x-rays upon the proliferation of various tissues. The critical dosage levels of the same quality of x-rays using the same dosage rate for proliferation *in vitro* of explants of one- and two-day-old rat kidneys lie between 90,000 and 95,000 r; for the spleen of the same rat they lie between 50,000 and 60,000 r; for Sarcoma 180, also between 50,000 and 60,000 r; for chick embryo heart, between 150,000 and 160,000 r.

The following characteristics were observed within the range of the critical dosages of x-rays: (1) There was not only a decrease in percentage of growing explants but also a decrease in size of the new-growth; (2) a latent period ranging from 48 to 72 hours, and (3) liquefaction of the nutritive medium.

Since these destructive phenomena are occurring within the critical dosages of x-rays, the importance of the determination of the range of these dosages for various types of tissues is evident. The factors controlling the critical doses of x-rays, as demonstrated in these experiments, are the exposure time and dosage rate. Consequently, the proper combination of both factors is important in achieving the best results.

The liquefaction of the nutritive medium which was produced in the cultures irradiated within the critical doses may be explained as follows: It is a well established fact that liquefaction is produced by dead tissues. There are two digestive actions by the enzymes within the cells: the catabolic and anabolic. The catabolic process predominates in the dead cell and results in a complete destruction or solution of the cells. The assumption that liquefac-

TABLE IX.—CRITICAL DOSAGE LEVELS OF X-RAYS FOR VARIOUS TISSUES GROWN *in vitro*

| Type of Tissue | Dosage Rate of X-rays in r/min. | Time of Radiation in Min. | Critical Loses in r Preventing Proliferation | Remarks |
|---|---|---|---|---|
| Rat Kidneys | 936 | 96–101 | 90,000 to 95,000 | Of explants irradiated with 70,000 r, 47.1 per cent produced growth of epithelia and fibroblasts during 24 hours' incubation |
| Rat Kidneys | 234 | 320–342 | 75,000 to 80,000 | Of explants irradiated with 70,000 r, only 11.1 per cent produced small growth of epithelia and fibroblasts during 72 hours' incubation |
| Rat Kidneys | 10,000 | 13–14 | 130,000 to 140,000 | Only very small growth or single scattered cells occurred during 48 to 72 hours' incubation |
| Chick Embryo Heart | 936 | 150–160 | 140,000 to 150,000 | Only single scattered cells could be observed in some of the cultures |
| Chick Embryo Heart | 10,000 | 25–26 | 250,000 to 260,000 | Only single scattered cells were observed in the irradiated cultures |
| Rat Spleen | 936 | 53–64 | 50,000 to 60,000 | Only small growth of fibroblasts and a few scattered round cells occurred during 48 hours' incubation |
| Sarcoma 180 | 936 | 53–64 | 50,000 to 60,000 | The newgrowth of the irradiated explants was much smaller and thinner than that of the control cultures |
| Sarcoma 180 | 10,000 | 8½–9 | 85,000 to 90,000 | Only one out of 27 irradiated explants produced small growth of new cells |

tion of the nutritive medium was produced by the dead cells, which possibly had a short life, due to the effect of irradiation, is justified. Since higher doses are required to inactivate the enzyme activities within the cells, in order to prevent mitosis, the destructive effects produced by the doses of x-rays employed in these experiments are not directly upon the enzymes but rather upon the other constituents within the cells.

Some speculations on the mechanism of the time factor and latent period are offered: In considering the biologic effects of irradiation on the cells, the apparent importance of the time factor strongly suggests the existence of sensitive phases during cell division. That is, if we assume that the destructive effects of irradiation are considerably more effective during a relatively short period in the life cycle, then we have a basis for assuming that a smaller dosage rate with a correspondingly longer period of exposure would increase the probability of direct hits during these sensitive periods, thereby decreasing the total dosage for a given biologic effect. The results obtained with two different dosage rates of the same quality of x-rays, as recorded in Tables I and II and demonstrated in the graph (Fig. *B*), support this view.

Which is the most sensitive phase during cell division, due to a given dose of radiation, remains to be proven. Regaud regards the prophase and anaphase in tissues as the most sensitive phases; Holthusen, the anaphase in *Drosophila* eggs, while Mottram found the metaphase in *Ascaris* to be the most vulnerable to a given dose of radiation. Sachs, in his most recent publication (2), suggests the prophase in *Tradescantia* microspores as the most appropriate for intermittent radiation of low intensity in producing sufficient breaks in the nuclei to prevent normal cell division. There may exist during the process of mitosis of various cells a different sensitivity to a given dose of radiation. There is, however, a general agreement that cells in process of division are more sensitive than are cells in the resting state, which is in accordance with the interpretation of the results of our experiments.

In regard to the latent period, the following assumptions can be considered: (1) The x-ray hits may occur in a less sensitive phase of cell division, so that a certain process of recovery takes place; (2) secondary chemical changes as a consequence of the first biologic changes produced by ionization, as assumed by the ionization theory of Dr. Failla, and (3) irradiation within certain dosage levels produces an effect not only upon the viability but also upon the reproductive capacity of the cells.

In reference to the difference in susceptibility of the nutritive medium and of the tissue itself to a given dose of radiation, the following observations were made: Chick embryo heart irradiated with 30,000 r and left in the irradiated medium did not produce any growth of new cells, as recorded in our previous publication (1). However, a fairly good growth occurs during 24 hours of incubation when the irradiated explants were transferred immediately after irradiation to a freshly prepared medium. As recorded in Table IV, the critical dose of filtered x-rays for chick embryo heart was found to be about 150,000 r, using a dosage rate of 936 r/min. Accordingly, the dose of x-rays necessary to prevent the proliferation of chick embryo heart is about five times greater than that required for inactivation of the nutritive medium, in other words, for the growth-promoting substances. The critical dose of the same type of x-rays for one- to two-day-old rat kidney was found to be about 90,000 r, and for the spleen of the same rat, as well as for Sarcoma 180, about 60,000 r. Accordingly, the proportions of these doses to that of 30,000 r for the nutritive medium will be about 1 : 3 and 1 : 2, respectively. In any case, a smaller dose of filtered x-rays is required to inactivate the nutritive medium than to prevent the proliferation of the tissue itself. Consequently, the sublethal and lethal doses for various tissues, as recorded in the previous publication (1), have to be

referred to the growth-promoting substances and not to the proliferations of tissues. These observations may also serve as further evidence that the effect of irradiation upon the proliferation of various tissues *in vivo* is not direct, but rather indirect, as stated heretofore (4).

Previously (3 and 4) it was shown that a much higher dose of x-rays is required to effect the metabolic changes of various tissues than is necessary to prevent proliferation. These observations were substantiated in our most recent investigations, of which only one example will be mentioned here. A dose of 300,000 r applied during 30 minutes of exposure, using a dosage rate of 10,000 r/min., did not affect either the oxygen intake or the ærobic glycolysis of rat kidneys, although a dose of 150,000 r of the same type of x-rays prevented the proliferation of this type of tissue.

Although fragments of freshly excised tissues have been used as test subjects in order to apply the experimental conditions *in vitro* closer to those applied for therapeutic purposes *in vivo*, the doses of x-rays preventing proliferation of tissues as demonstrated in these experiments are far in excess of those which are tolerable *in vivo*. However, through experimentation with excised tissues, eliminating the blood, lymph, nerve, and other systems present in the living organism, we may obtain a better understanding of the factors controlling growth processes. The characteristics produced by various doses and dosage rates of x-rays upon tissues *in vitro*, such as the relation of the time intensity factor, the selective action of x-rays, the latent period, the liquefaction of the nutritive medium, could not be determined through experimentation *in vivo*. However, they indicate the actual effects produced by radiation upon the physiologic processes, and therefrom conclusions for practical application may be drawn.

The experimental approach, as well as the test subjects used in these experiments, differ from those used by other investigators. A comparison of results obtained is, therefore, unfeasible.

Acknowledgment: I wish to thank Ira I. Kaplan, M.D., Director of Division of Cancer, Department of Hospitals, New York City, and Frank CoTui, M.D., Director of the Surgical Research Laboratory, New York University Medical College, for their kind interest in making this work possible. My grateful appreciation is also expressed to Carl B. Braestrup, Physicist for the Division of Cancer, Department of Hospitals, New York City, and his associates, particularly to Gordon H. Cameron, for their helpful advice and assistance; to Shering and Glatz, Inc., for financial aid, and to the W.P.A. for a technical helper assigned to me for these experiments.

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# THE ADDITIVE EFFECTS OF RADON AND NEUTRAL RED UPON *CHAOS CHAOS*[1]

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IN THE present investigation, during observations of irradiated ameba, *Chaos chaos*, subjected to roentgen rays or to radon emanations, food vacuole formation, and digestion appear to be in no way inhibited by radiation. With this in mind, cultures of *Chaos chaos* were stained with weak solutions of neutral red (Koehring, 10) for several days before irradiation. The stained vacuoles and the behavior of newly formed vacuoles were carefully watched for many days after irradiation. No abnormal staining or vacuole behavior was observed, and no abnormal functioning of digestion or of proteolytic enzymes could thus be suspected. Heavy dosages of radiation—up to 10,000 roentgen units delivered in one dose, and 4,225 millicurie-hours of radon—do not prove to be directly harmful to weakly stained or to unstained amebæ.

The relation of short wave radiation to enzymes *in vitro* is problematical, with some evidence that irradiated enzymes are partially inactive (Schomer, 21). Reports of irradiation of enzymes *in vivo* have not been found in the literature. Radiation sickness has been attributed partially to stimulation of enzymes which produce tissue autolysis (Martin and Mousund, 13).

Neutral red combines with proteolytic enzymes without inactivating them. Used as a vital stain for animal and plant tissues, the dye is of low toxicity, in the same sense that it does not readily produce inhibiting and lethal effects. Nevertheless, it is a foreign substance, and, as such, it gives some unmistakable evidence of cellular stimulation (Koehring, 10). The initial effects, especially as the dye is being concentrated by the cell, may produce stimulation as increased vacuole activity. Roffo and Correa (19) found no increase of carbon dioxide production when neutral red was used in tissue cultures of chick embryonic hearts, rat spindle-cell sarcoma, and rat carcinoma. (Methylene blue under the same conditions increased carbon dioxide, and other dyes inhibited growth.)

Therefore, instead of staining cultures several days previous to irradiation, dye and radon needles were added to small cultures at the same time. The cultures were irradiated in heavy glass inkwells of

[1] Accepted for publication in August, 1939.

TABLE I.—*Chaos chaos* SUBJECTED TO RADON EMANATIONS

| Date | Amount of Radon | Culture | History | Survival | Mc.-hr. Exposed |
|---|---|---|---|---|---|
| 7/16 | 9.6 mc. | 20 c.c. | In good condition, with feeding, until hot weather (32° C.+), Aug. 3. Controls survived hot weather | 18 days | 1,113 |
| 7/19 | 38 mc. | 10 c.c. | In good condition, with feeding, until hot weather (32° C.+), Aug. 6. Controls survived only a few days longer | 18 days | 4,223 |
| 8/ 1 | 12 mc. | 5 c.c. | In good condition until Aug. 12 (not fed). Few and pale, widespread forms on Aug. 18, very active. Culture destroyed. Controls also poor | 18 days | 1,388 |
| 8/ 1 | 9 mc. | 10 c.c. | In very good condition until Aug. 17. Few large, pale forms on Aug. 22. Not enough food. Controls same | 22 days | 994 |
| 8/18 | 20 mc. | 5 c.c. | In good condition, with feeding. Large, pale, sprawling forms to date | Indef. | 2,464 |

The first three of these cultures had neutral red-stained amebæ from a culture stained July 6. The others had one pipetteful each from the survivors of the stained stock culture which remained a very rich culture. In preparing small cultures for irradiation amebæ were always mixed from several stock cultures. *Paramecium* and *Blepharisma* grew in the cultures as food for the amebæ.

TABLE II.—*Chaos chaos* SUBJECTED TO RADON AND NEUTRAL RED AT THE SAME TIME

| Date | Amount of Radon | Culture | History | Survival | Mc.-hr. Exposed |
|---|---|---|---|---|---|
| 8/21 | 46 mc. | 10 c.c. | Stained with neutral red about 1:1,000,000<br>Aug. 22: Round, dark red, small, slow. Only fragments of amebæ<br>Aug. 23: Dark red, brown fragments. Fragments alive(?). Dead bodies<br>Aug. 24: Completely disintegrated. No bodies, no fragments | 2 days | 1,168 |
| *RT* = 23–24° C. | | | | | |
| 8/25 | 21 mc. | 10 c.c. | Stained with neutral red about 1:1,000,000<br>Aug. 26: Round, knobbed or clubbed; quiet; dark red. Many fragments<br>Aug. 27: Very dark or else very pale fragments. Some fragments active with streaming. No normal forms<br>Aug. 28: All bodies completely disintegrated | 3 days | 1,060 |
| *RT* = 23–24° C. | | | | | |
| | | 10 c.c. | Controls stained 1:1,000,000. Alive, large and normal. Kept until Sept. 10 | Indef. | |
| 8/26 | 15 mc. | 10 c.c. | Stained with neutral red about 1:500,000<br>Aug. 27: Dark, rounded or clubbed fragments. Slow, quiet<br>Aug. 28: A few dark, very small fragments. Other black, dead bodies<br>Aug. 29: All bodies completely disintegrated | 3 days | 759 |
| *RT* = 22–23° C. | | | | | |
| | | 10 c.c. | Controls stained with neutral red 1:500,000. Alive, large and active to date | Indef. | |
| 8/29 | 24 mc. | 10 c.c. | Radon controls—no stain (to repeat earlier observations). Slightly smaller than normal. Some more pale. Spreading and active. Alive to date | Indef. | 2,865 |
| *RT* = 18–19° C. | 17 mc. | 10 c.c. | Stained with neutral red 1:500,000<br>Aug. 30: Fair condition; many small forms moving, dark red. Many fragments, dark red to brown, quiet<br>Aug. 31: Same—more fragments. All small. No normal sized amebæ although some are active, either very dark or very pale. Many have food vacuoles<br>Sept. 3: One active form found. Other fragments all very dark or pale lobes. No viable forms(?) | 6 days | 1,364 |
| | 13 mc. | 10 c.c. | Stained with neutral red 1:500,000<br>Same as above with 17 mc. Very little difference between the two cultures<br>Sept. 5: All bodies completely disintegrated | 7 days | 1,100 |
| | | 10 c.c. | Controls stained 1:500,000. In good condition to date | Indef. | |
| 9/2 | 20 mc. | 10 c.c. | Control radon—no stain. Sprawling, active but smaller forms than normal. Some are clumped but become active when placed on slide and spread wide with many pseudopods. In good condition to date | Indef. | 2,464 |
| *RT* = 18–19° C. | | | | | |
| | 19 mc. | 10 c.c. | Stained with neutral red 1:1,000,000<br>Sept. 5: Many very large, moving forms. The fragments are large, rounded, and dark. In fair condition<br>Sept. 7: Fragments—none viable. No pale forms. All are brown to black, ragged. No membranes visible, only coagulated masses. Majority disintegrated | 5 days | 1,360 |
| | 16 mc. | 10 c.c. | Stained with neutral red 1:1,000,000<br>Sept. 5: Same as 19 mc. culture with perhaps more larger forms<br>Sept. 7: Same as 19 mc. Coagulated masses, irregular and fuzzy outlines. Many disintegrated | 5 days | 1,146 |
| | 13 mc. | 10 c.c. | Stained with neutral red 1:500,000<br>Sept. 5: In much worse condition than the 19 mc. and 16 mc. cultures. Fragments only—fairly large, dark<br>Sept. 6: A few fragments which could not possibly survive. Most bodies are entirely disintegrated | 4 days | 806 |
| | | 10 c.c. | Controls stained 1:500,000. In good condition to date | Indef. | |
| 9/6 | 24 mc. | 10 c.c. | Stained with neutral red 1:500,000<br>Sept. 7: Very much fragmented. Few fragments | 3 days | 1,215 |

from 200 to 290 c.c. volume. The glass radon needle (tube with wall thickness of 0.2 mm.) was dropped directly into the culture, allowing for both the beta and gamma factors of the emanation, most of the alpha particles being excluded. The inside measurements of the wells averaged 3 cm. in diameter and 3.5 to 4 cm. in depth; the cultures averaged from 10 to 12 c.c. of medium, with 40 or more large *Chaos chaos* per culture.

The experiments are listed in Tables I and II.

Within 24 hours it is apparent that amebæ subjected to both neutral red (1:1,000,000 or 1:500,000 conc.) and to continuous radon irradiation labor under difficulties. Food vacuole formation continues; dense red bodies of old vacuoles are present and new, colorless vacuoles forming around live, still motile food organisms are frequently observed. The amebæ then cease to appear normal with the following deviations.

*Size.*—The tendency is toward smaller and smaller organisms, such as the amebæ bud, many of which live for a time while others rapidly become colorless and die within a few hours. Small portions budded and remaining for a time, as well as the larger remnants of amebæ, appeared as dark fragments, slowly ameboid in early stages, quiet in later stages.

*Color.*—Neutral red stains the granules of amebæ in the concentrations used in this investigation, as well as the food vacuoles. In the control stained amebæ the granules are pink-red in that range of the dye which may indicate from *p*H 5–6.9. The granules are distinct and discrete. A few bright, clear orange granules, probably indicating *p*H 7.1–8, are always present. In the irradiated dyed organisms the granules tend to become fuzzy in outline, ranging from a dull brick-red to brown-red in color. Brick-red is the neutral, *p*H 7, color of the dye, but the brown color cannot be interpreted for *p*H values.

When the stained and irradiated amebæ round up or clump in briefly lobed or knobbed form, they appear as ragged, dense masses of dark red to brown granules. Before disintegration they may spread out as pale streams of sparsely granulated protoplasm; or else, remaining dense in a central portion, form blisters before death.

There is nothing distinctive in the proto-

TABLE II.—*Chaos chaos* SUBJECTED TO RADON AND NEUTRAL RED AT THE SAME TIME (*Cont.*)

| | | | | | |
|---|---|---|---|---|---|
| *RT* = 18–19° C. | | | appear able to survive, yet a few fair sized amebæ with food vacuoles are active<br>Sept. 9: No viable fragments. Disintegrating bodies | | |
| | 13 mc. | 10 c.c. | Stained with neutral red 1:500,000<br>Sept. 7: Larger amebæ than fragments. Fair shape. Dark, quiet, yet some are forming new food vacuoles<br>Sept. 9: Much fragmentation, yet a few still mobile and fair sized with food vacuoles<br>Sept. 10: Only fragments | 5 days | 931 |
| | 12 mc. | 10 c.c. | Stained with neutral red 1:250,000<br>Sept. 7: Fragmented. Many bodies disintegrating. Others are dark masses with fuzzy outlines. A few small amebæ with food vacuoles<br>Sept. 9: A few viable fragments. Disintegration<br>Sept. 10: No viable fragments | 4 days | 746 |
| | | 10 c.c. | Controls stained with neutral red 1:500,000<br>Sept. 7: Excellent condition. Many food vacuoles<br>Sept. 10: Excellent condition. Many food vacuoles | Indef. | |
| | | 10 c.c. | Controls stained with neutral red 1:250,000<br>Sept. 7: Excellent condition. New vacuoles being formed. Some viable fragments—small<br>Sept. 10: Small but active and full of food vacuoles | Indef. | |

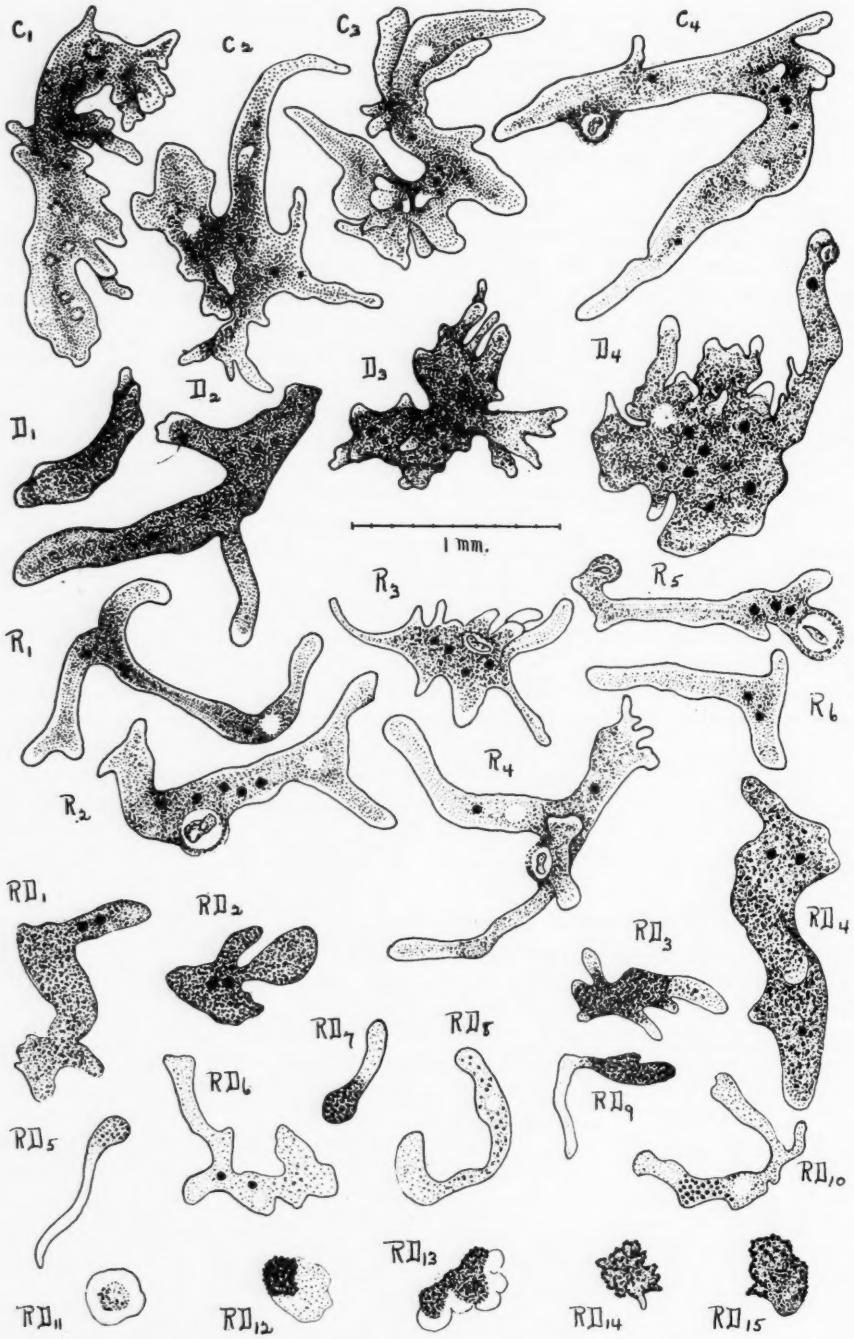


Fig. 1. Camera lucida drawings.

*C* 1–4, controls—normal *Chaos chaos*.

*D* 1–4, dye controls—amebæ stained with **neutral red** 1:500,000. Temporary abnormalities appear in contrast with normals.

plasmic conditions in which these fragments die; no definite conclusions may be drawn regarding coagulation states and increase or decrease of viscosity. In the struggle to maintain normal conditions, a coagulated condition may prevail and death may occur in that state with the disintegration of a dense, black mass. Or, budding and blistering may proceed swiftly without coagulation, and myriads of pale to colorless globules be fragmented before the organism succumbs as a final exhausted fluid mass enclosed in a delicate film.

The one important fact noted in all these observations is that the cell must be able to form new membranes as well as to restrict membrane formation, if it is to survive. The irradiated controls (not stained) are amebæ which are temporarily almost universally smaller than the stock normals. Some division and some fragmentation occur during radon irradiation. (Counts have not been made in this preliminary study in which the attempt has been to irradiate fairly large cultures under conditions in which they might be kept for some time, and the presence of food material and débris prohibits accurate counting of organisms, especially of viable and nonviable budded fragments.)

Neutral red-stained controls (not irradiated) also tend to be smaller than normal, and fragments are observed in lively, flourishing cultures. (See $D_1$, Fig. 1, a viable bud.) Furthermore, neutral red tends to stimulate vacuole activity, which involves membrane invagination to form the vacuoles.

Irradiation effects of budding and dividing, plus the membrane formation stimulated by neutral red, prove to be too great a burden for the organism. Phenomena of membrane failures—excesses or inhibitions—appear to be involved in all the lethal states observed. Control of membrane formation, allowing for some budding and division, but rigidly restricting such activity, may be the basis of resistance.

No satisfactory conclusions may be drawn regarding the effect of radiation upon any enzymes of the organism. Decolorization of the vacuoles and granules does not occur; this presumably means that the enzymes which neutral red demonstrates are not inactivated (Koehring, 10). Increase of color in the coarsened granules of simultaneously irradiated and dyed amebæ and change from the *p*H range of the dye to other colors may mean increase of enzyme activity, with abnormal enzyme-substrate-activator relationships.

The conclusions which can be drawn are:

1. *Chaos chaos* is resistant to irradiation. This resistance is relative: among many protozoa which were irradiated, *Chaos chaos* was by far the *most sensitive*. In none of the experiments were *Paramecium* and *Blepharisma* killed, while cultures always remained full of smaller *Ciliates*, *Flagellates*, small, unidentified amebæ, and rotifers. However, *Chaos chaos*, a relatively small mass of protoplasm to contain so great a nuclear content, of from several hundred to a thousand nuclei, is radiosusceptible although much less so than would be expected. Marshak and Bollman (12) related the susceptibility of tissues to x-rays to their nuclear-cytoplasmic ratios. Other multinucleate forms, such as the bead-nucleate, *Stentor*, and *Spirostemum* are not sensitive and were not killed by irradiation in any experiments during this work. It is possible that that protozoan, with the greatest apparent nuclear-cytoplasmic ratio of the organisms studied, may prove to be most sensitive to radiation, thus bearing out the conclusions of Marshak and Bollman. (The actual nuclear-cytoplasmic ratio of *Chaos chaos* has not been measured.)

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*R* 1–6, radon controls—amebæ subjected to a 20 mc. glass radon tube for two days. Small size is the temporary abnormality.
*RD* 1–15, amebæ subjected to both radon (17 mc. radon tube) and neutral red (1:500,000) for two days. *RD* 1–4, motile; *RD* 5–10, dying and dead fragments; *RD* 11–15, dying and dead fragments.

2. *Chaos chaos* is resistant to neutral red, granular staining concentrations of the dye producing no permanent effects.

TABLE III.—*Chaos chaos* SUBJECTED TO SHORT INTENSE IRRADIATION

| Date | Amount of Radon | Culture | History | Survival | Mc.-hr. Exposed |
|---|---|---|---|---|---|
| 9/3 | 1,011 mc. | 20 c.c. | Given 10 minutes of radiation<br>Controls without stain<br>Sept. 7: Excellent condition. Very large<br>Sept. 10: Enormous—larger than controls! | Indef. | 168 |
| | 1,011 mc. | 20 c.c. | Given 5 minutes of radiation<br>Controls without stain<br>Sept. 7: Excellent condition. Very large<br>Sept. 10: Larger than controls! | Indef. | 84 |
| | 1,011 mc. | 20 c.c. | Given 10 minutes of radiation<br>Stained with neutral red 1:1,000,000<br>Sept. 7: Excellent condition. Very large<br>Sept. 10: Large, vigorous, full of food vacuoles | Indef. | 168 |
| | 1,011 mc. | 20 c.c. | Given 5 minutes of radiation<br>Stained with neutral red 1:1,000,000<br>Sept. 7: Excellent condition. Very large<br>Sept. 10: Large, vigorous, full of food vacuoles | Indef. | 84 |

*Note:* No stock culture amebæ were ever larger or more vigorous than these irradiated cultures.

3. To irradiation plus neutral red staining, *Chaos chaos* becomes much less resistant, and is then killed with appreciably smaller doses of radon emanation.

Additional work is necessary to study the details of the reaction of radon and neutral red on the cell. The immediate results, however, are striking enough to warrant the hypothesis that the use of neutral red may prove to be a safe and effective way of increasing radiosensitivity.

Russ and Scott (20) reported that trypan blue, injected either locally or into a distant part of the animal, markedly increased the sensitiveness of Rat Sarcoma F 16. Orr (1937) used phenol red to retard the proliferation of mouse sarcomas. Yet trypan blue and other dyes known to be more toxic for protozoa and tissue cultures than is neutral red may have undesirable effects. Andrevont (3) found that the subcutaneous injection of trypan blue lowered the resistance of mice to transplantable and induced tumors.

From many studies of tissue cultures it is well known that normal tissue as well as tumor tissue can be readily stained with neutral red with no injurious effects (Belkin and Shear, 5).

Also, neutral red has been used clinically to such an extent that it is recognized as non-toxic. Since the work of Winkelstein and Marcus (25), numerous clinicians have used injections of neutral red solutions in the study of stomach and kidney function (Afanasev, 1; Allodi and Quaglia, 2; Arezzi, 4; Bobbio and Arezzi, 6; Dias-Amado, 9; Machline and Gorbouncova, 11; Morrison, Gardner, and Reeves, 15; Oliva y Marra López, 16; Polichetti, 17; Riggio, 18; Trapani, 22; Vegetti, 23; Vitale, 24). Neutral red in a 1 per cent solution is injected in the treatment of generalized leprosy (Montel and Truong-van-Que, 14).

Thus, the use of neutral red, as one of the least toxic dyes known, may prove to be an aid in the radiation of cells when it is desirable that the radiosensitiveness be increased.

The writer wishes to express gratitude to Shields Warren, M.D., for making it possible to carry out these experiments.

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# "KNOW THYSELF"[1]

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THIS was a common saying of the Greek philosopher Socrates. But even though his career ended with the drinking of the "poison hemlock" more than 2,300 years ago, this aphorism had been handed down to him by earlier sages. It seems quite evident that not long after the dawn of what we call civilization, the peculiar workings of the human mind were already recognized. In this day of bigger and better deficits, when we are the sole possessors of noble purposes and only the other fellow occupies the citadel of greed, it behooves us to view ourselves in the mirrors of the past and present and once again strive to learn what manner of man we really are.

For the past one hundred and fifty years each generation has witnessed a more rapid advance in the vistas of knowledge and a greater improvement in living conditions than the previous generation. This has tended to produce an attitude of smug complacency, a feeling that our problems are different from what they have ever been before, and that the past has no lessons for us. It is true there has been a change of scenes and a shifting of scenery, perhaps with resulting improvement, but has there been a change for the better in the quality of the actors who play the drama of life? That is very much open to question.

In the days when Greek civilization was in its flower, the meager information available was for the most part in the hands of a small percentage of the population. With the advent of the printing press the stage was being set for an accumulation and dissemination of knowledge such as had never been possible previously. Investigations throughout the world could now serve as building stones for further researches. The hoi polloi began to have access to a wealth of knowledge which previously had been denied even to the few.

The acquisition of education, the possession of so-called knowledge, is not, however, synonymous with the power to think and to reason. All that should be necessary to convince one of this are the futile political mass movements which take place in response to economic tides or demagogic appeals to prejudice.

The men who do constructive thinking and who blaze the trail into new vistas of knowledge are still relatively few, just as was the case in past ages. It is true that they have pyramided knowledge and scientific advances at an amazing speed. But when their meager information and opportunities are considered, the conclusions reached by the early Greek philosophers and scientists are even more wonderful. Over 2,500 years ago a theory of evolution amazingly similar to that which we accept to-day was being advanced. About a century later Anaxagoras proposed a conception of matter which only recently has been proven true. Doubtless most of you are aware that a search of the medical writings of Hippocrates has revealed evidence that he knew not a few of the things which have been re-discovered in recent years. The intelligentia of those days made wonderful use of their knowledge and observations, quite as brilliant as manifested in our own time. They leave us little excuse for an egotistical belief in the greater capacity of the human mind of to-day.

Throughout recorded history, in spite of different religious beliefs, strikingly similar codes of ethics have existed among various tribes and nations of people. During periods when the distribution of wealth is fairly equitable and the majority must struggle hard for a livelihood, man exhibits his most generous impulses and his closest observance of his moral codes. But even then, this observance is confined to his

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

own group, tribe, or nation. Up to the present this has not spread beyond national boundaries. *A propos* of this, is that blot on our own history, our consistent record of broken promises with the Indians whom we treated in the characteristic way strong nations use in dealing with weak, alien peoples. Much as we may wish to think so, it would appear that moral codes have not formulated a way of life in response to our religious convictions, but have rather evolved out of the exigencies of group survival.

By nature, man is a rather lazy animal. The necessity to work for a livelihood has always played an important part in the development of his character. We struggle because of our relative insecurity in an attempt to make our future more certain. If he thinks he is secure, man in the aggregate will not struggle. Thus, early in life, habits of industry and self-reliance, or their converse, are acquired and developed.

In the early days of Greek and Roman civilization property was rather evenly distributed and the fight for existence was the common lot of nearly every man. Religion played a large part in the lives of men, and moral standards and ethical ideals were in the ascendancy. Due to the development of commerce in Greece, wealth gradually became concentrated in the hands of a few. Later, trade combined with the loot of conquest brought similar results to Rome. Then envy, greed, and selfishness, which earlier had been partly submerged in the common struggle, came to the forefront. Through the power of wealth the rich exploited the poor. The poor eked out a miserable existence, and eventually rebelled and started the class war. Such contest tends to undermine character, but there is one thing even more demoralizing to man. The politicians of the time furnished this crowning achievement. They arranged to have the State underwrite the livelihood of the poor and thereby removed the necessity to struggle. Under the required taxation to support this system, enterprise was stifled and business languished. The self-supporting classes no longer had the incentive to work. Man gradually lost his stamina and virility. Morals ebbed and religion became decadent. Finally Greece fell, and later Rome. Then came the Dark Ages.

The parallelism between those times and the present is uncomfortably striking. Just as in the earlier ages, man now seems incapable of profiting from the lessons of the past. He continues to create the problems which plague him. Thus history inevitably repeats itself. One must needs wonder, however, if our wonderful scientific achievements and labor-saving devices may not be serving to increase the tempo of this cyclic change which has doubtless many times been the lot of man.

The statement is made that of all forms of government a democracy is the best, but it is also the most difficult to maintain. It has without doubt proven a good means of utilizing human selfishness for improving the average economic status of society. Through the agency of private initiative, man's industry and creative instincts are best developed. Under the aegis of such liberty idealism finds a fertile field in which to grow. As wealth accumulates, greed and selfishness begin to crowd out that sense of fair play so essential to the proper functioning of a democracy. The many checks and balances in our Constitution show plainly that its framers were good philosophers, and that they well realized the dangers to democratic government inherent in the vagaries of human nature. The agencies of government can, however, to a limited degree only, hold in check these baser impulses of man. Justice must largely spring spontaneously from his better nature. Politicians seem unaware of this fact. Their answer to the problems created by human selfishness is to make government more restrictive of individual liberty and more complex, until it finally falls of its own weight.

Before this kind of gathering, little reason would exist for such a discussion, were a special effort not made to ascertain the rating of that species of *Homo sapiens* known as physician, and in particular that

sub-species known as radiologist. How does he play the game and is he really sapient?

During the past fifty years the practice of medicine has been undergoing rapid metamorphosis, not only in its scientific aspects, but also in the attitude of the physician toward his profession. Not so many years ago nearly all rural communities had easy access to medical care. The physician may not have been well equipped scientifically, but he largely made up for this in a willingness to devote his life to hard work and real service for a modest income. The rapid accumulation of wealth and the improved standards of living, especially in cities, has exercised a somewhat baneful effect on the medical profession, as it has in other walks of life. The willingness to serve a community for a small income has been supplanted largely by a desire to get a good share of this world's goods without commensurate effort. As a result, rural areas are frequently poorly served and the price often prohibitive, because of their distance from a physician.

The rapid growth of specialization, which has spread quite beyond the bounds of reason, has, in part, come in response to the same impulses. The surgeon was the first specialist upon the scene and therefore quite easily assumed the rôle of the plutocrat of medicine. Soon the rising generation of physicians began in large numbers to turn toward the "land flowing with milk and honey." In due time so crowded was the field that the number of necessary operations became rather insufficient to go around. Accordingly, there have doubtless been many, many cases in which the budding young surgeon, and often the older one as well, has stretched his imagination to the breaking point in deciding that an operation was necessary. Probably no other specialty has felt the effects of overcrowding to the same extent, but all of them can bear witness to the increasing avarice of the physician.

In other respects our code of ethics has been strained severely in the last two generations. Formerly physicians held rigidly to the rule that advertising in any form was a severe breach of our rules of conduct. In recent years publicity has been resorted to more and more as a means of attracting patients to individual physicians or groups. Not the least of these schemes for obtaining business is locked up in that expression so often heard: "I wanted to find out for sure what was wrong, so I went to the Clinic." It is true that groups of physicians working together can often render better service to patients and may aid greatly in advancing the science of medicine. One must needs wonder, however, if some of these groups have not brought about a lowering of ethical standards quite sufficient to counteract any scientific gains made.

Our own specialty has not been entirely free from attempts to persuade the world to beat a pathway to our doors. Quite a few higher voltage machines have in recent years been installed to the accompaniment of considerable fanfare. No one denies the need for a thorough study of the efficacy of these shorter wave lengths, but the purpose of such installation is sometimes not inspired either by a desire to advance science or better serve the patient.

Thus in many ways the physician shows the same disintegrating effects now prevalent in all society. We still talk of our code of ethics and of the ideals of medicine, but more and more we accord them only lip service. As we ponder over the Hippocratic oath, can we help but wonder if the torch of idealism may not have burned more brightly in his day than now.

Even before "the times were out of joint," more or less agitation had started concerning the high cost of medical care. The source of this ferment largely reposed in some of those busy-bodies whose social security was well guaranteed and whose existence was quite apart from the struggling human current. Thus detached from the world of reality, such beings not only "hitch their wagon to a star," but rise with it into the starry spaces of fond illusion. Their type has always been with us. They were not alien to Greece or Rome.

Sometimes they appear in the garb of statesmen, or should I say, politicians; others play the rôle of teachers; and, not so long ago, there arose from our own ranks the self-anointed four hundred.

Unfortunately there are germs of truth in their contentions. In many ways we have encouraged practices which in recent years have needlessly increased the cost of sickness care. Probably the most glaring example is the unnecessary use of the hospital. All too often the patient is put there "to be worked out," as goes the common expression, when a thorough examination in the office might have accomplished the same result with much less expense, but harder work for the physician. The field of obstetrics shows most vividly this trend. Not many years ago a large percentage of deliveries were carried out in the home, while to-day many obstetricians, in spite of the not infrequent spread of contagion in the hospital, insist on doing all of their deliveries there at much greater expense. Can anyone deny that the fundamental cause for this is our desire to make our living easier? Yet, what seems to be our answer to this? Hospital insurance, so there can be still more hospitalization.

In our anxiety to get ahead of our fellow practitioners we often incur an overhead which has slight justification as far as the public interest is concerned. Yet the public must inevitably pay. The unnecessary privately owned hospital is a good case in point. Still there are occasional extenuating circumstances springing from a sometimes hypocritical exclusiveness of certain hospital staffs. In our own specialty when, for competitive purposes, we install expensive equipment beyond the requirements of adequate service or proven therapeutic results, we thereby deny to the public as economical service as they are entitled to receive.

In addition to the overhead of physical equipment we must not forget that the capital investment in education plays a certain part in the cost of medical care. The incentive to the many financially barren years of study is that ultimately our emolument may be the greater. This is as true of medicine as of other learned professions. Shortly after the turn of the century the American Medical Association began its campaign to improve medical standards. That such a step was much needed and in the interest of both the public and the profession, no one can deny. In more recent years the further extension of the period of medical training has sprung partly from self-interest, from an attempt to prevent overcrowding of the profession. It is not my purpose to suggest that this increased training is undesirable or to imply, as some have, that it has deprived the country districts of physicians. It is rather to point out that we have hereby increased the cost of medical care for largely selfish reasons rather than through purposeful actions from the standpoint of public interest.

During the past few years the various specialties, including our own, have been laboring over the problem of standardization. The conclusion reached seems to be that three years of special training, following a regular internship, will be required for those who enter our specialty. Again more non-productive years of education! Is self-interest entering into these requirements? Are we not actuated in part by the desire to make it hard for others to get in? It is not my intention to advocate that so much training is unnecessary, but rather to ask this question: With our economic wheels already creaking, can society afford to have every specialist so well trained that he can recognize nearly every rare condition before he starts upon his career? And after all, may we not be allowing ourselves to exaggerate the capacity of the human mind?

In the boom years of 1928 and 1929 when our national productivity was at its highest, the average income for each individual was only about $640 per year. This would amount to a little over $2600 per average family. It is appreciably lower now. If we are able to earn it, we can rightfully lay claim to a greater than average income because of our years of non-

productive special training. But this much is certain: It is most unwise as well as unfair in these times to try to push our income far above the average, if we have to do so by imposing undue hardships on the moderate and low income classes. Unfortunately we often place the profession in a rather unfavorable light because we are too much concerned with what we will receive for our services and too little with what people can afford.

To-day when we are caught in the maelstrom of regimentation and so-called social security, our reactions continue to be anything but purposeful. Instead of fighting against the current and trying to keep individuals in the self-sustaining, self-respecting class at perhaps some personal sacrifice, we are too willing to let them slip into the charity group. When politicians plan to spend money, which we do not have, for more free medical care, we can only visualize the harmful effects on ourselves and our profession and not the degenerating effects on society. We seem to have failed to grasp that socialized medicine is only one symptom of that dread disease —paternalism.

In our attempt to combat the wiles of politicians, we have at times been led like "babes in the wood " For years we have been pointing out that socialized medicine in England and Germany increased morbidity. This increase is well known to arise largely from compensation for loss of wages during sickness. Just about the most potent remedy known to man has for some time been demonstrated in England, where astounding immediate cures result at the end of six months when the compensation is cut in half. Our experience with Workmen's Compensation Insurance and with the non-cancellable disability insurance would also seem to indicate quite clearly what happens when individuals think their security is guaranteed. Yet, our House of Delegates not long ago unreservedly approved the principle of compensation for loss of wages during sickness. Not only that, but they also put forward the curious assertion that such compensation had a distinct influence toward recovery and tended to reduce permanent disability. Since no agency but the government could be foolish enough to write such insurance, how could we travel a faster road to State-controlled medicine? It would appear that there is much room for more sound thinking in facing our problems.

The most important step in that direction is to analyze carefully the motives which actuate us. There is little to suggest that we can materially change our nature. All too often, however, we exercise so little intelligence that self-interest defeats its own purpose. If our education and experience as physicians have made any sound contribution to our ability to reason, we should the better safeguard our own interests by tempering selfishness with enlightenment.

We, together with the rest of society, need to engage in much introspection. Self-analysis is the only pathway by which we can hope to eradicate the sham, the pretense, the hypocrisy, the loose thinking which is so prevalent to-day. The saying "know thyself" is as full of meaning now as it ever was in the painfully slow forward march of man.

DISCUSSION

LOWELL S. GOIN, M.D. (Los Angeles): It seems to me appropriate that we pause in the midst of such a feast of scientific information and knowledge as is being spread before us to look briefly at life through the eye of the philosopher. Since the world we live in is not the pleasant, interesting world of scientific radiologic knowledge that we are immersed in temporarily, but an actual, tangible, concrete world of reality, we should take care to indulge in our introspective study and reflection—not in our character of physicians, no matter how important that consideration may be —but in our character as men, as citizens of our nation and of the world.

We must avoid, or, if we have them already, we must abandon, the various false concepts which Dr. Myers has called to our attention. We must refuse to be swayed

by propaganda, no matter how plausible it seems to be. We must fight and overcome injustice, no matter how mitigating the accompanying circumstances may seem to be.

The all too prevalent concept of democracy as a wholesale scramble for privileges without entailing any reciprocal obligations; our concept of individualism as unlimited self-indulgence without any consideration for its effect upon group effort and group life; the instinct, apparently ever-increasing, to look to the State to solve every problem and to meet every emergency; the terrifying superficiality of modern education; the systematic prolongation of youth and the period of irresponsibility; our lax attitude toward crime and our soft, muddle-headed view that criminals and enemies of society are in the main pitiable creatures in the grip of circumstances beyond their control; that feeling of pacifism which, in general, is only a vague and poorly reasoned notion that there is nothing in this world worth heroic sacrifice, these are the concepts that we must abandon and these are the trends which Plato described as "the infallible signs of decay in the societies of free and self-governing men."

# CASE REPORT

## DOUBLE GALL BLADDER

### A CASE REPORT

*By* LLOYD BRYAN, M.D., *San Francisco*

The occurrence of double gall bladder in man has been recognized since 31 B.C., when Pliny described a case in a sacrificial victim, and the first case was recorded in medical literature by Blasius, in 1674.

The number of cases reported in the modern literature totals less than forty. In 1926, Boyden reviewed the literature and recorded twenty cases and there have been additional case reports by Nichols, Climan, Cave, Hayes, Slaughter and Trout, Weiss, Wilson, and Gross, who, in 1936, published a comprehensive review of the subject of anomalies of the gall bladder and duct. Only eight cases are recorded which have been demonstrated roentgenologically and on account of the rarity of the condition it seems justifiable to report the following case.

Mrs. H. J. M., widow, aged 70 years (referred by A. E. Gauthier, M.D.), complained of dull aching pain in the left lower quadrant, and pain and tenderness over the left sacro-iliac joint.

Several years ago a diagnosis of low grade chronic cholecystitis had been made. X-rays taken at this time (no dye was used) were negative for gallstones.

This dull pain in the left lower quadrant had persisted for the past several weeks. There was no apparent relation to the ingestion of food; no radiation; no history of constipation or diarrhea. There was occasional nausea without vomiting. Stools were negative for blood. There was marked flatulence. A barium enema at this time revealed many small diverticula in the descending colon. Recently the pain had appeared in the epigastrium and the right upper quadrant. The patient noted that the lower abdominal pain was worse when her back condition was aggravated.

Examination was essentially negative except for persistent tenderness in the right upper quadrant and over the descending colon. There was considerable tenderness over the left sacro-iliac joint, which was aggravated by movement. The urinalysis was negative; temperature normal; pulse 76, regular; blood pressure 130/78; hemoglobin 85 per cent; weight 142 pounds.

The patient was examined at 15, 17, and 19 hours following oral administration of four grams of sodium tetra-iodophenolphthalein. The greatest concentration was obtained at the 19-hour period and two gall bladders with distinct cystic ducts were demonstrated. It was not possible to determine whether or not the two cystic ducts united before joining the common duct. Both gall bladders showed a prompt response to a fat meal and were entirely empty of dye at the third hour.

450 Sutter Street

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Fig. 1.

# THE PROFESSIONAL BUREAU OF THE COLLEGE

This is a progress report. It covers the period between the February, 1940, meeting of the Board of Chancellors, in which it was decided to expand the activities of the Professional Bureau, and the June, 1940, meeting. A preliminary report appeared in the April issue of this Bulletin.

The expansion, as outlined in the previous report and which was authorized by the Board of Chancellors, has been completed. Printed forms including all biographical data as to education and training of applicants have been made available and distributed to all applicants and to the department heads of the 88 approved radiological training centers. In addition, forms have been printed for the use of institutions or individuals seeking a radiologist. On these forms, essential data are recorded, showing financial arrangement, type of practice, equipment, whether or not the institution has had a radiologist.

Publicity articles were prepared and submitted to the Executive Secretary for distribution to hospitals and medical periodicals or wherever he deemed it essential that publicity should be given to the Professional Bureau. At the present time, the Bureau has 73 applicants. These may be tabulated as follows: Protestant, 40; Jewish, 22; Catholic, 7; Mormon, 1; Quaker, 1; Diplomates of the Board, 21; not Diplomates, 52. Financial arrangement preferred: salary, 28; percentage, 22; rental, 6; salary and percentage, 14. Expected income:

| | |
|---|---|
| $2,000 | 1 |
| 2,500 | 5 |
| 3,000 | 8 |
| 3,500 | 12 |
| 4,000 | 12 |
| 4,500 | 2 |
| 5,000 | 15 |
| More than $5,000 | 6 |
| Not stated | 10 |

Locality preferred: South, 5; North, 2; Midwest, 12; East, 5; Pacific Coast, 10; Southwest, 5. Full-time, 64; part-time, 5; private practice, 2; would open private office, 2; has had position: yes, 32; no, 41. Interested in vacancy: in 1940, 53; 1941, 12; 1942, 8.

Letters received from institutions seeking applicants seem to indicate a definite trend toward full-time radiology and a complete divorce from part-time radiology practice in those institutions seeking a radiologist. Some of them frankly state that the staff is not satisfied with the pure film-reading service and no consultation which they are receiving. Some state that it is poor from a financial standpoint, and some feel that, as a matter of competition, they must have a full-time radiologist.

Referring to the March 30, 1940, hospital number of the *Jour. Am. Med. Assn.* we find that there has been an increase in the number of hospitals with approved radiological departments at the rate of one hundred per year. This also shows an increase in a five-year period of seven hundred physician-radiologists in charge. This evidently means that the five hundred installed during the five-year period took on a radiologist and about two hundred had the department turned over to some physician in order that they might have a physician-director.

In the classification of residencies and fellowships, it shows that 49 men were in training in radiology in 1927, 66 in 1934, 110 in 1937, and 245 in 1940. Under "Departments of Radiology," the study shows that departments in charge of physician-radiologists have increased, from 1934 to 1940, from 3,563 to 4,249. It is, therefore, evident that, excluding a certain number of approved radiologists who are, for statistical purposes, carried as in charge or director of the department in these hospitals, there are many such departments in charge of men who are not Diplomates of the Board. In view of the fact that there are 245 men now in training who are potential job-seekers, it is quite evident that some of these men will have to be displaced in favor of full-time and well trained young radiologists.

It will be noted that the largest number of applicants are willing to start on a salary

basis. In a recent survey conducted by the Pennsylvania State Radiological Society, it was found that the average income of radiologists on straight salary was $4,200 per year, and of those on a commission basis, income average was $7,600 per year. It will also be noted that more than half of the applicants are expecting less than the minimum salary found in this survey.

Since expansion of the Bureau, upon receipt of an opening, all applicants and all department heads are notified. A letter has been written to each of the openings, asking what response has been received to notices sent out by the Bureau. Some have replied that they have had as many as 20 replies from our applicants, and every letter has been enthusiastic about the service rendered by the Professional Bureau and the number of responses that they have had due to contacts we have been able to give them with men looking for locations.

There has been some misunderstanding among some of the men as to the functions of the Professional Bureau. A number of them have referred men seeking a residency in radiology to us. We have also had some requests for residents and have attempted to bring both parties together. This seems a better method than a blunt refusal in such cases.

At the present time, the liveliest interest shown by institutions seeking radiologists is from the State of West Virginia. This is evidently due to knowledge of the existence of the Bureau being disseminated among hospitals in that particular locality. It is obvious when one reads the advertisements of commercial bureaus that all men seeking positions and all institutions seeking radiologists have not appealed to us, although there are undoubtedly some duplications. This is no implication that we expect to monopolize the placing of radiologists, but is used only as an indication that our publicity has not been fully effective.

It is not the purpose of this report to burden you with statistics, but a project like the Professional Bureau yields statistical information that is of value from the economic side of the practice of radiology. An attempt was made to evaluate or predict revenue from radiologic work in certain localities. This was brought about by the information we received in which it was clearly shown that the amount of work done in a locality or in an institution had no relation to the number of admissions or to the population. In earlier figures, it seemed that one could estimate that the potential revenue for radiologic work should be about one dollar per year per person.

Unfortunately, it is impossible to obtain accurate information pertaining to the total gross charges for radiologic work in communities of representative size.

Gross income for radiologists, as revealed by the economic survey conducted by the Inter-Society Committee last year, proved it to be below that for orthopedic surgery, surgery, or proctology. This survey also showed the highest income in the East South-central region and the lowest in New England. The ratio of radiologists to population is highest in the East South-central, 1 : 124,000. In New England it is 1 : 48,000. This shows a correlation between the average population per radiologist and the average gross income for radiologists. By dividing the population per radiologist by the gross income of radiologists, we get an average expenditure per person for radiology in the East South-central region of 12 cents and in New England, 18 cents. Carrying these figures further with the figures compiled by group hospital and sickness insurance plans and their calculated days of illness and expenditure for medical services, we come to the conclusion that about 75 cents per capita will be the expenditure for radiology in a prosperous community, down to 50 cents, or less, in the impoverished areas.

It is also a significant fact, obtained from information sent to us pertaining to openings and the salary offered, that in those institutions where the salary range for radiologists is around $2,500 a year, we will find that x-ray examinations have a ratio to the admissions of 1 : 2 plus, while in those institutions desiring a higher class man, the ratio will be 1 plus : 1. From this, one arrives at the conclusion that the amount of radiologic work done in an institution is directly proportionate to the caliber of the radiologist, and, obviously, a man's income is directly proportionate to his ability. I am of the opinion that sufficient evidence can be collected to bear out these suppositions (obtained from a small amount of material) that this information will be enlightening to those hospitals desiring to hire radiologists at a technician's salary. Further statistics along this line will be compiled as available information presents itself and we hope to incorporate such figures in a future report.

S. W. DONALDSON, M.D., *Director*

# RADIOLOGICAL SOCIETIES IN NORTH AMERICA

*Editor's Note.*—Will secretaries of societies please cooperate with the Editor by supplying him with information for this section? Please send such information to Leon J. Menville, M.D., 1201 Maison Blanche Bldg., New Orleans, La.

## UNITED STATES

### CALIFORNIA

*California Medical Association, Section on Radiology.—Chairman,* Karl M. Bonoff, M.D., 1930 Wilshire Blvd., Los Angeles; *Secretary,* Carl D. Benninghoven, M.D., 95 S. El Camino Real, San Mateo.

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*Los Angeles County Medical Association, Radiological Section.—President,* M. L. Pindell, M.D.; *Vice-president,* Richard T. Taylor, M.D.; *Secretary,* Wilbur Bailey, M.D., 2007 Wilshire Blvd.; *Treasurer,* Henry Snure, M.D., 1414 South Hope Street; Kenneth Davis, M.D., *Member of Executive Committee.* Meets second Wednesday of each month at County Society Building.

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*Pacific Roentgen Society.—Chairman,* William E. Costolow, M.D., Los Angeles; *Members of Executive Committee,* I. S. Ingber, M.D., San Francisco; D. R. MacColl, M.D., Los Angeles, and J. D. Coate, M.D., Oakland; *Secretary-Treasurer,* L. Henry Garland, M.D., 450 Sutter St., San Francisco. Executive Committee meets quarterly; Society meets annually during annual meeting of the California Medical Association.

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*San Francisco Radiological Society.—Secretary,* Harold A. Hill, M.D., 450 Sutter Street. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (Univ. of Calif. Med. School) and for the second six months at Lane Hall (Stanford Univ. School of Med.).

### COLORADO

*Denver Radiological Club.—President,* N. B. Newcomer, M.D., 306 Republic Bldg.; *Vice-president,* Elizabeth Newcomer, M.D.; *Secretary,* Paul R. Weeks, M.D., 520 Republic Bldg.; *Treasurer,* L. G. Crosby, M.D., 366 Metropolitan Bldg. Meets third Friday of each month at homes of members.

### CONNECTICUT

*Connecticut State Medical Society, Section on Radiology.—Chairman,* Owen J. Groark, M.D., 881 Lafayette St., Bridgeport; *Secretary-Treasurer,* Max Climan, M.D., 242 Trumbull St., Hartford. Meetings twice annually in May and September.

### DELAWARE

Affiliated with Philadelphia Roentgen Ray Society.

### FLORIDA

*Florida Radiological Society.—President,* J. H. Lucinian, M.D.; *Vice-president,* John N. Moore, M.D.; *Secretary-Treasurer,* Elliott M. Hendricks, M.D., 314 Sweet Bldg., Fort Lauderdale. Meetings held in November and at the annual meeting of the Medical Association of Florida in the spring.

### GEORGIA

*Georgia Radiological Society.—President,* Robert Drane, M.D., DeRenne Apts., Savannah; *Vice-president,* J. J. Collins, M.D., Archbold Hospital, Thomasville; *Secretary-Treasurer,* Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

### ILLINOIS

*Chicago Roentgen Society.—President,* Adolph Hartung, M.D.; *Vice-president,* Warren W. Furey, M.D.; *Secretary,* Chester J. Challenger, M.D., 3117 Logan Blvd. The Society meets at the Palmer House on the second Thursday of October, November, January, February, March, and April.

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*Illinois Radiological Society.—President,* Harry W. Ackeman, M.D., 321 W. State St., Rockford; *Vice-president,* D. R. Hanley, M.D., St. Mary's Hospital, Streator; *Secretary-Treasurer,* William DeHollander, M.D., St. John's Hospital, Springfield. Meetings quarterly by announcement.

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*Illinois State Medical Society, Section on Radiology.—Chairman,* Warren W. Furey, M.D., 6844 Oglesby Ave., Chicago; *Secretary,* Harry W. Ackeman, M.D., 321 W. State St., Rockford.

### INDIANA

*The Indiana Roentgen Society.—President,* H. H. Inlow, M.D., Shelbyville; *President-elect,* Charles Wyeth, M.D., Terre Haute; *Vice-president,* C. A. Stayton, M.D., Indianapolis; *Secretary-Treasurer,* Clifford C. Taylor, M.D., 23 E. Ohio St., Indianapolis. Annual meeting in May.

### IOWA

*The Iowa X-ray Club.*—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

### KENTUCKY

*Kentucky Radiological Society.—President,* D. B. Harding, M.D., Lexington; *Vice-president,* I. T. Fugate, M.D., Louisville; *Secretary-Treasurer,* Joseph C. Bell, M.D., 402 Heyburn Bldg., Louisville. Meeting annually in Louisville, third Sunday afternoon in April.

### MAINE

*See* New England Roentgen Ray Society.

MARYLAND

*Baltimore City Medical Society, Radiological Section.—Chairman,* Harold E. Wright, M.D., 101 W. Read St.; *Secretary,* Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MASSACHUSETTS

*See* New England Roentgen Ray Society.

MICHIGAN

*Detroit X-ray and Radium Society.—President,* O. J. Shore, M.D., 552 Fisher Bldg., Detroit; *Vice-president,* Clarence E. Hufford, M.D., 421 Michigan St., Toledo, Ohio; *Secretary-Treasurer,* E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

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*Michigan Association of Roentgenologists.—President,* J. H. Dempster, M.D., Detroit; *Vice-president,* L. E. Holly, M.D., Muskegon; *Secretary-Treasurer,* J. E. Lofstrom, M.D., 1536 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

*Minnesota Radiological Society.—President,* Harry Weber, M.D., Mayo Clinic, Rochester; *Vice-president,* G. T. Nordin, M.D., Minneapolis; *Secretary,* John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

*The Kansas City Radiological Society.—President,* L. G. Allen, M.D., 907 N. 7th St., Kansas City, Kansas; *Secretary,* Ira H. Lockwood, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

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*The St. Louis Society of Radiologists.—President,* Oscar C. Zink, M.D., St. Luke's Hospital; *Secretary,* Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of October, January, March, and May, at a place designated by the president.

NEBRASKA

*Nebraska Radiological Society.—President,* Roy W. Fouts, M.D., 1007 Medical Arts Bldg., Omaha; *Secretary,* D. Arnold Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

(Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island.) *Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW HAMPSHIRE

*See* New England Roentgen Ray Society.

NEW JERSEY

*Radiological Society of New Jersey.—President,* James G. Boyes, M.D., 912 Prospect Ave., Plainfield; *Vice-president,* Nathan J. Furst, M.D., 190 Johnson Ave., Newark; *Secretary,* W. James Marquis, M.D., 198 Clinton Ave., Newark; *Treasurer,* H. A. Vogel, M.D., 1060 East Jersey St., Elizabeth, and *Counsellor,* H. J. Perlberg, M.D., 921 Bergen Ave., Jersey City. Meetings at Atlantic City at time of State Medical Society, and Midwinter in Newark as called by president.

NEW YORK

*Associated Radiologists of New York, Inc.—President,* I. J. Landsman, M.D., 910 Grand Concourse, New York City; *President-elect,* D. E. Ehrlich, M.D., 35 West 92nd St., New York City; *Vice-president,* Frederic E. Elliott, M.D., 122 76th St., Brooklyn; *Treasurer,* Solomon Fineman, M.D., 133 East 58th St., New York City; *Secretary,* William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

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*Brooklyn Roentgen Ray Society.—President,* A. L. L Bell, M.D., Long Island College Hospital, Henry, Pacific, and Amity Sts.; *Secretary-Treasurer,* L. J. Taormina, M.D., 1093 Gates Ave. Meetings first Tuesday in each month at place designated by president.

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*Buffalo Radiological Society.—President,* Edward Koenig, M.D., 100 High St., Buffalo; *Vice-president,* W. Roger Scott, M.D., 598 Pine St., Niagara Falls; *Secretary-Treasurer,* Joseph S Gian-Franceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

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*Central New York Roentgen Ray Society.—President,* Albert Lenz, M.D., 613 State St., Schenectady; *Vice-president,* Dwight V. Needham, M.D., 123 Sedgwick St., Syracuse; *Secretary-Treasurer,* Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

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*Long Island Radiological Society.—President,* Samuel G. Schenck, M.D., Brooklyn; *Vice-president,* G. Henry Koiransky, M.D., Long Island City; *Secretary,* Marcus Wiener, M.D., 1430 48th St., Brooklyn; *Treasurer,* Louis Goldfarb, M.D., 608 Ocean Ave., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

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*New York Roentgen Society.—President,* Henry K. Taylor, M.D., 667 Madison Ave., New York City;

*Vice-president*, Roy D. Duckworth, M.D., 170 Maple Ave., White Plains, N. Y.; *Secretary*, Eric J. Ryan, M.D., St. Luke's Hospital, New York City, and *Treasurer*, Paul C. Swenson, M.D., 168th St. and Broadway, New York City.

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*Rochester Roentgen-ray Society.—Chairman*, George H. S. Ramsey, M.D., 277 Alexander St.; *Secretary*, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

*Radiological Society of North Carolina.—President*, Robert P. Noble, M.D., 127 W. Hargett St., Raleigh; *Vice-president*, A. L. Daughtridge, M.D., 144 Coast Line St., Rocky Mount; *Secretary-Treasurer*, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meetings with State meeting in May, and meeting in October.

OHIO

*Ohio Radiological Society.—President*, U. V. Portmann, M.D., Cleveland; *Secretary*, J. E. McCarthy, M.D., Cincinnati. A committee was appointed to draw up a constitution and by-laws. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

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*Cleveland Radiological Society.—President*, L. A. Pomeroy, M.D., Hanna Bldg., Cleveland; *Vice-president*, P. C. Langan, M.D., 215 Wellsley Ave., Akron; *Secretary-Treasurer*, H. A. Mahrer, M.D., 10515 Carnegie Ave., Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

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*Radiological Society of the Academy of Medicine* (Cincinnati Roentgenologists).—*President*, Samuel Brown, M.D.; *Secretary-Treasurer*, Justin E. McCarthy, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

*Pennsylvania Radiological Society.—President*, H. Norton Mawhinney, M.D., Pittsburgh; *President-elect*, Peter B. Mulligan, M.D., Ashland; *First Vice-president*, Harold S. Callen, M.D., Bradford; *Second Vice-president*, Harold W. Jacox, M.D., Pittsburgh; *Secretary-Treasurer*, L. E. Wurster, M.D., 416 Pine St., Williamsport; *Editor*, William E. Reiley, M.D., Clearfield; *Assistant Editor*, Sydney J. Hawley, M.D., Danville; *Censor for Three Years*, A. R. Snedden, M.D., McKeesport. The Society meets annually; time and place of next meeting will be announced later.

The annual meeting of the Pennsylvania Radiological Society was held at Hotel Hershey, Hershey, Pa., Friday and Saturday, May 17 and 18, 1940. The meeting was called to order by the President Louis A. Milkman, M.D., presiding. In addition to the two-day scientific session, consisting of papers and exhibits by members of the Society, W. Edward Chamberlain, M.D., of Philadelphia, gave an interesting talk on "Fractures." Another highlight of the meeting was a talk on "Massive Dose Roentgen Therapy of Superficial Malignancies," by B. P. Widmann, M.D., of Philadelphia.

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*The Philadelphia Roentgen Ray Society.—President*, Jacob H. Vastine, II, M.D., Medical Arts Bldg., Philadelphia; *Vice-president*, A. Maxwell Sharpe, M.D., 708 Sproul St., Chester; *Secretary*, Barton R. Young, M.D., Temple University Hospital, Philadelphia; *Treasurer*, Fay K. Alexander, M.D., Chestnut Hill Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

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*The Pittsburgh Roentgen Society.—President*, Paul G. Bovard, M.D., 306 Corbett St., Tarentum, Pa.; *Vice-president*, John H. Gemmell, M.D., 262 Connecticut Ave., Rochester, Pa., and *Secretary-Treasurer*, Harold W. Jacox, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings held second Wednesday of each month at 4:30 P.M., from October to June, at various hospitals designated by program committee.

RHODE ISLAND

*See* New England Roentgen Ray Society.

SOUTH CAROLINA

*South Carolina X-ray Society.—President*, T. A. Pitts, M.D., Columbia; *Secretary-Treasurer*, Malcolm Mosteller, M.D., Columbia Hospital, Columbia. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

SOUTH DAKOTA

Meets with Minnesota Radiological Society.

TENNESSEE

*Memphis Roentgen Club.*—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

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*Tennessee Radiological Society.—President*, Eugene Abercrombie, M.D., 305 Medical Arts Bldg., Knoxville; *Vice-president*, Christopher C. McClure, M.D., 404 Doctors Bldg., Nashville; *Secretary-Treasurer*, Franklin B. Bogart, M.D., 311 Medical Bldg., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

*Texas Radiological Society.—President*, C. F. Crain, M.D., Corpus Christi; *President-elect*, M. H. Glover, M.D., Wichita Falls; *First Vice-president*, G. D. Carlson, M.D., Dallas; *Second Vice-president*, P. E.

Wigby, M.D., Dallas; *Secretary-Treasurer*, L. W. Baird, M.D., Scott and White Hospital, Temple. Meets annually. The next annual meeting is to be Jan. 18, 1941, in Sherman.

VERMONT

*See* New England Roentgen Ray Society.

VIRGINIA

*Radiological Society of Virginia.—President*, Fred M. Hodges, M.D., 100 W. Franklin St., Richmond; *Vice-president*, L. F. Magruder, M.D., Raleigh and College Aves., Norfolk; *Secretary*, V. W. Archer, M.D., University of Virginia Hospital, Charlottesville.

WASHINGTON

*Washington State Radiological Society.—President*, H. E. Nichols, M.D., Stimson Bldg., Seattle; *Vice-president*, George Cornett, M.D., Yakima; *Secretary-Treasurer*, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

*Milwaukee Roentgen Ray Society.—President*, H. W. Hefke, M.D.; *Vice-president*, Frederick C. Christensen, M.D.; *Secretary-Treasurer*, Irving I. Cowan, M.D., Mount Sinai Hospital, Milwaukee. Meets monthly on first Friday at the University Club.

*Radiological Section of the Wisconsin State Medical Society.—Secretary*, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

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*University of Wisconsin Radiological Conference.—Secretary*, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

*Section on Radiology, Canadian Medical Association.—Chairman*, Gordon Richards, M.D., Medical Arts Bldg., Toronto; *Secretary*, W. J. Cryderman, M.D., Medical Arts Bldg., Toronto.

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*Section on Radiology, Ontario Medical Association.—Chairman*, E. H. Shannon, M.D., St. Michael's Hospital, Toronto; *Secretary*, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

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*Canadian Association of Radiologists.—President*, J. E. Gendreau, M.D., Montreal; *Vice-president*, W. H. McGuffin, M.D., Calgary; *Honorary Secretary-Treasurer*, W. L. Ritchie, M.D., Montreal; *Chairman of Interrelations Committee*, G. E. Richards, M.D., Toronto.

# EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

## SUMMATION OF DOSAGE

In a small sample of American roentgen therapists, one in six—when they were treating multiple fields—took the sum of the dosage applied to each field and added them all together, recording, sometimes in red ink, the "total roentgens." In cases, this ran up to 9,000 roentgens.

Such a widespread misconception as to the nature of our unit of dosage needs correction, it seems to me. It appears obvious to me that a single 10 × 20 cm. area gets the same dose when treated for, say, ten minutes as a single 10 × 20 area, that it does when treated, first, one 10 × 10 area for ten minutes and then the other 10 × 10 area for ten minutes. Cross-fire beams can really be summed only in terms of tissue dose within the tumor, not as the surface dose of the various portals of entry.

Suppose one is making photographs on an eight-exposure roll of film. Suppose he exposes one roll of film, outdoors, one-hundredth of a second for each of the eight exposures, and they come out all right. Suppose in the next roll he exposes only two, and then, being impatient to see the results, develops the whole roll without waiting for pictures for the other six places on the film. Surely you would not consider his roll of film under-exposed.

What I have presented above need not contradict, I think, the following accepted fact:

There is a real clinical difference between the treatment of one 10 × 10 area with 1,000 roentgens in a two-week period, and the treatment of two such areas by the same dose and the same time. There is also a clinical difference between the treatment of one 10 × 10 area to a total of 1,000 roentgens in two weeks' time and the treatment of a 15 cm. square area to the same dose in the same time. When one is dealing with areas differing very greatly, irradiated to the same total number of roentgens measured in the beam in air, there is both a physical and a clinical difference. The physical difference depends upon the difference in the amount of back-scatter effective in the area irradiated. The clinical difference consists in this, namely, that the skin and subcutaneous tissues can recover from a greater amount of roentgen injury when the area injured is small, due to the proximity of surrounding uninjured tissue with its normal blood supply. Moreover, the systemic damage done by heavy irradiation, *i.e.*, the roentgen sickness, is correlated with the total volume of patient irradiated, and so, of course, is greater for large areas and for multiple areas.

In recording roentgen dosage, therefore, we ought to sum up the roentgens applied to each area treated for the whole series of treatments, but not to add together the dosage for separate areas.

*San Francisco* R. R. NEWELL, M.D.

## ANNOUNCEMENTS

### THIRD ANNUAL REFRESHER SERIES

*Annual Meeting, Dec. 2–6, 1940*

The Third Annual Refresher Series, Postgraduate Courses, offered by the Radiological Society of North America, will be presented Sunday, Dec. 1, through Friday, Dec. 6, 1940.

The courses will occupy five hours on Sunday and two hours, from eight to ten, each morning of the meeting.

The plan of presentation will follow closely that employed at the Atlanta meeting and the number of courses will be somewhat increased.

The Executive Committee has ruled that there will be no charge for enrollment for members and their guests. A complete and detailed announcement, together with an enrollment blank, will be published in an early issue of RADIOLOGY.

## THE AMERICAN COLLEGE OF RADIOLOGY

The following new officers were elected at the annual meeting of the American College of Radiology, held at the Commodore Hotel in New York City on June 12, 1940: *President*, Henry J. Walton, M.D., Baltimore, Md.; *Vice-president*, Sherwood Moore, M.D., St. Louis, Mo.; *Chairman, Board of Chancellors*, Vincent W. Archer, M.D., University, Va. New members of the Board of Chancellors elected for a four-year term were: Lewis G. Allen, M.D., Kansas City, Kansas, and George E. Pfahler, M.D., Philadelphia. Hollis E. Potter, M.D., Chicago, was re-elected *Treasurer*, and Mr. Mac F. Cahal was re-elected *Executive Secretary*.

The next annual meeting of the College will be held at Cleveland on Wednesday during the week of the American Medical Association meeting.

# COMMUNICATION

## UNIVERSITY OF PENNSYLVANIA'S CYCLOTRON

Plans for construction of a cyclotron for use primarily in medical research at the University of Pennsylvania, made possible by a gift of $200,000 from William H. Donner, retired industrialist, and providing the basis for a line of research believed to hold substantial promise for the study and treatment of cancer, were announced by President Thomas S. Gates of the University last night. The gift raises Mr. Donner's total contribution to the University's Bicentennial Fund to $400,000.

Weighing 250 tons and capable of projecting particles of matter with a velocity of 25,000 miles a second, sufficient to carry them from the earth to the sun in an hour, Pennsylvania's cyclotron will be only the third of its size in the world, matching in capacity the largest now in operation, which is in the laboratory of Dr. E. O. Lawrence, at the University of California. The second cyclotron of this size is now under construction in the Department of Terrestrial Magnetism of the Carnegie Institution in Washington.

Already possessed of a 5,000,000-volt electrostatic generator, installed last year as an adjunct of the Department of Physics, the University of Pennsylvania will be the first university in the world to have at its disposal all of the powerful research tools provided by a combination of these two kinds of "atom-smashers," each of which has distinct advantages over the other for different kinds of investigation.

Mr. Donner designated his gift for the cyclotron as an addition to his contribution of an equal amount in 1937 to establish the William Henry Donner, Jr., Department of Radiology, in memory of his son. The cyclotron will be installed in a specially constructed building adjoining the Department of Radiology, in the rear of the new unit of the University Hospital now under construction on the south side of Spruce Street between 34th and 36th Streets.

Measuring about 16 by 6 feet at the base and 12 feet high, the apparatus will consist primarily of a huge steel magnet and a round, flat vacuum chamber, placed between the pole pieces of the magnet. The vacuum chamber contains two hollow, D-shaped electrodes, arranged back to back, between which the atomic projectiles are accelerated.

In operation of the cyclotron, atoms of heavy hydrogen will be piped to the center of the vacuum chamber through a tube containing also a tungsten filament. Electrons discharged by the incandescent filament will tear from a certain proportion of the heavy hydrogen atoms, as they emerge from the tube, the single electron each contains, leaving only their positively charged nuclei, which are known as deuterons and consist of one proton and one neutron each. These deuterons, being charged, will be caught in the magnetic and electric field within the electrodes and accelerated in ever-widening circles by alternating positive and negative charges, introduced into the electrodes by a powerful short wave transmitter.

After about forty circuits in their spiral course, during which their speed will be boosted by a "kick" from the generator twice in each circuit, or a total of eighty times, the deuterons will reach the outer edge of the vacuum chamber, where they will be deflected by a charged plate into a gun-like projector. If uninterrupted they would stream from this tube as a beam of blue light, with an energy far greater than that of most lightning flashes.

For the treatment of cancer, two technics will be principally employed: first, the bombardment of various chemicals which, thus being rendered radio-active, can then be administered to patients; second, the direct application to the patient of a beam of neutrons,

produced by placing in the target chamber at the end of the projector a plate of beryllium, from which the neutrons, released by the bombardment, stream directly into the cancerous tissue.

The latter technic, being one for which few facilities are available in other places, and consequently one whose possibilities have been less explored, will at the beginning, at least, engage the principal interest of the University's radiologists. Having been compelled to limit the therapeutic use of his cyclotron at the University of California to two days a week, due to the demands of various fields of physical research, Dr. Lawrence, with whom Mr. Donner consulted before making the gift to Pennsylvania, has expressed his pleasure at the prospect of more intensive studies of direct therapy.

For therapeutic work, the energy of Pennsylvania's cyclotron will be equivalent to that of about two hundred pounds of radium—a staggeringly great quantity when it is considered that there are in the world less than two pounds of radium that have been purified, that hospitals fortunate enough to possess any radium whatever list their treasure in terms of thousandths of a gram, and that the substance bears a money value of from $20,000 to $25,000 a gram and would be worth about $10,000,000 a pound if such a quantity could be purchased.

The beam of neutrons released by bombardment of beryllium is also believed to have distinct advantages over x-rays. In treatment of some kinds of cancer, the efficacy of neutrons has been found to be about five times as great as million-volt x-rays. Experience to date indicates that neutrons have a much higher rate of selectivity between normal and abnormal tissue, as well as a much greater power of penetration. Neutrons enter the cancerous tissue and release within it electrons of 3,000,000 volts energy, or three times the energy with which the electrons producing million-volt x-rays leave their source.

The potential benefits of this new cancer therapy and research program will be enhanced by Pennsylvania's operation of the new Foundation for the Study of Neoplastic Diseases, established at the University last month by the Penn Mutual Life Insurance Company to co-ordinate and compare the various methods and results of cancer treatment in all divisions of the University Hospital and to make available the soundest possible laboratory and clinical data.

Another significant advantage lies in the activity of the Eldridge R. Johnson Foundation for Research in Medical Physics at the University of Pennsylvania, which, it is expected, will both serve and be served by the new research program in the Department of Radiology.

Although the study and treatment of cancer for which the cyclotron will be used will be the primary objective, in accordance with the interest which chiefly motivated Mr. Donner in making the gift, it will be possible to use the apparatus concurrently for the benefit of such departments of the University as those of physiology, biology, botany, research medicine, physics, and chemistry.

One phase of the program which will be second only to cancer study in importance will be the preparation of "tagged" atoms, by means of which physiologists hope ultimately to learn the exact distribution in the various body tissues of all the many chemical elements they absorb from food and other sources. A little is already known, such as the fact that iodine is absorbed by the thyroid gland, and calcium and phosphorus by the bones. Such knowledge will be helpful in directing to cancerous tissues certain elements which are known to be absorbed by them, and which have first been rendered radio-active by bombardment in the cyclotron.

What is known of chemical distribution in the body, however, is considered very little in contrast with what has yet to be learned. Knowledge in this field may be greatly expanded by introducing various radio-active elements into the body, one at a time, and tracing each with an electroscope or a Geiger counter, which will detect and measure the radiations emitted by the element being studied when the recording instrument encounters the tissue by which that element has been absorbed. Through this procedure physiologists may discover the route and destination of each element entering the body, the duration of its retention by the tissue, and something of its function.

Although the cyclotron is less suitable than the electrostatic generator for determining the precise data required for pure research in physics, due to variations in the velocity of the charged particles composing the beam it projects, the efficiency of Pennsylvania's cyclotron in producing radio-active materials will be about two hundred times that of the electrostatic generator, this greater efficiency resulting from

higher energy and a much higher rate of production of charged particles.

Anticipating an immediate beginning on preliminary work for the installation, Dr. A. N. Richards, vice-president of the University in charge of medical affairs; Eugene P. Pendergrass, M.D., head of the Department of Radiology, and Dr. Gaylord P. Harnwell, head of the Department of Physics, are planning a visit to Dr. Lawrence's laboratory at Berkeley, California, to study at first hand the installation there and the results which have been obtained with it.

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# IN MEMORIAM

## WILLIAM WALLACE BUFFUM

William Wallace Buffum, of Montclair, N. J., died Saturday, June 22, 1940, at the age of 52 years, after a brief illness.

Mr. Buffum was born at Friendsville, Penna., and at a very early age in life he demonstrated an unusually keen analytical mind which was to serve him a most useful purpose in his long executive career. He truly represented the typical American man, who, by his own initiative and hard work rose to a high position of trust in the scientific world. While he was not a scientist in the true sense of the word, the contact and the financial aid he was enabled to extend to scientific institutions, etc., gave him valuable information concerning the practical application of scientific knowledge such as few laymen possessed.

His first important contact with Mr. Francis Garvan was made in 1917, when he became affiliated with the Alien Property Custodian's office, in Washington, headed by Mr. Garvan, who subsequently became the President of the Chemical Foundation, Inc., which institution was faithfully served by Mr. Buffum for many years as its Business Manager. Through this connection with the Foundation he became business manager of the following well known national journals: *The American Journal of Cancer*, *The Journal of Clinical Investigation*, and *The Sewerage Works Journal*.

Through his influence the Chemical Foundation financed several cancer research works; also, large sums of money were contributed to universities for scientific investigation. His interest in cancer dates back many years, and it was partly through this interest that the Chemical Foundation contributed certain financial help to RADIOLOGY, official Journal of the Radiological Society of North America, for the purpose of disseminating cancer knowledge throughout many countries. In this manner he became well known and friendly to members of the radiological profession.

Mr. Buffum is survived by his widow, two sons, and one daughter.

LEON J. MENVILLE, M.D.

*New Orleans, La.*

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Percy J. Delano, M.D., of Chicago
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Lester W. Paul, M.D., of Madison, Wisc.
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## THE SPINAL CORD

Tumors of the Spinal Cord: Diagnosis and Treatment. Alfred W. Adson. Canadian Med. Assn. Jour., **40,** 448–454, May, 1939.

Tumors arising from tissues surrounding the spinal cord have been designated as "extramedullary," those in the cord itself "intramedullary." Symptoms of extramedullary tumors may be divided into three phases: first, involvement of nerve roots which may precede other symptoms by months or years; second, compression of the spinal cord, and third, a clinical picture of transverse section of the cord. Intramedullary tumors rarely produce pain but pass directly into the second symptomatologic phase. Sensory and motor disturbances are progressive until a definite transverse level becomes evident.

Examination includes comprehensive history, general and neurologic examination, and roentgen films of the spinal column, with or without iodized oil.

In the routine x-ray examination of the spine, the author believes evidence of pressure erosion is seen in vertebral pedicles, laminal, lateral, and spinous processes before erosion in the bodies of the vertebræ is manifest. Fluoroscopic study and films with heavy radiopaque oil have furnished much additional information. Intramedullary tumors are identified by division of the oil into two currents, one on each side of the cord. Extramedullary tumors usually produce a definite arrest of the flow of oil. If there is no tumor or cord compression, oil descends and remains permanently in the sacral *cul-de-sac*.

In the differential diagnosis, the following are to be considered: metastatic lesions, hypertrophic pachymeningitis, meningomyelitis, Pott's disease, spondylolisthesis, Paget's disease, subacute combined degeneration of the spinal cord, locomotor ataxia, syringomyelia, multiple sclerosis, and protruded intervertebral discs.

Of primary intraspinal tumors, 80 per cent are operable. After symptoms of compression have developed, a successful removal usually results in complete recovery. Immediate and careful investigation of every patient who presents symptoms of root pain or compression is imperative. After paralysis has occurred, the prognosis is less favorable.

M. L. Connelly, M.D.

## THE STOMACH

Prolapse of the Gastric Mucosa. Vincent W. Archer and George Cooper, Jr. Southern Med. Jour., **32,** 252–256, March, 1939.

Four proved cases of gastric mucosa prolapsing through the pylorus are presented. The symptoms of most significance are major hemorrhage, partial pyloric obstruction, or an anemia, the result of continued oozing.

The roentgenographic finding, following a barium meal, is a central negative shadow or filling defect in the duodenal cap, round or lobulated, containing a central streak of barium which represents the pyloric canal. The defect is best seen by pressure to partially empty the duodenal bulb.

A prolapsed gastric polyp presents the same picture. Roentgenographic findings may be absent. The treatment, if symptoms warrant, is surgical.

John M. Miles, M.D.

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Gastroscopic Study Compared with Other Methods of Diagnosis in Gastric Lesions. Elmer B. Freeman. Jour. Am. Med. Assn., **112,** 217–222, Jan. 21, 1939.

This study was made of 200 patients and in many of these two, three or more gastroscopic examinations were made on the individual patient. The study included a group of normal subjects, a group in which the digestive symptoms were considered functional, a group in which symptoms were thought to be due to chronic gastritis, a group with definite symptoms of gastric ulcer, and a group with symptoms thought to be due to gastric carcinoma. Two groups were studied after either pyloroplasty or posterior gastro-enterostomy: one in which the gastric symptoms were completely relieved and one in which partial relief or no relief had been obtained. A group of gastric hemorrhage cases in which all other methods of investigation had failed to disclose an organic basis for the bleeding was also studied.

The diagnosis of chronic gastritis must be made from the gastroscopic and x-ray observations, the former being the more important.

The various changes in color and general appearance of the mucosa, changes in size and shape of the mucosal folds, and the presence and the amount of thick, tenacious mucus adhering to the gastric wall determine the diagnosis of chronic gastritis, chronic superficial gastritis, chronic atrophic and chronic hypertrophic gastritis. Gastric ulcer and carcinoma of the stomach have characteristic appearances by which they may be recognized.

The procedure is helpful diagnostically in the study of gastric disease; it bears a supplementary relation to the other diagnostic methods but does not replace any one of them.

Charles G. Sutherland, M.D.

## SYPHILIS

Syphilis of the Lung: A Report of Three Cases Observed in North China. C. K. Hu, C. N. Frazier, and C. K. Hsieh. Chinese Med. Jour., **56,** 431–440, November, 1939.

Although pulmonary syphilis was recognized about a century ago and has been recorded by many, its occurrence is still doubted by some observers, because it is rare and its diagnosis difficult.

The writers set forth the following requirements to be fulfilled before diagnosis of syphilis of the lung can be accepted: (*a*) The patient must be proved to have syphilitic infection by a good venereal history, specific signs of the disease, and by serologic or other laboratory tests; (*b*) tuberculosis, pneumonia, and other conditions which might give rise to physical and roentgenologic changes simulating those of pulmonary syphi-

lis must be carefully ruled out by clinical and laboratory methods, and (*c*) the pulmonary lesion, if not entirely due to scars, should readily respond to antisyphilitic therapy, or to the finding of characteristic syphilitic lesions in the lung at necropsy.

Three cases that fulfill these requirements are presented and analyzed. While it is true that syphilis of the lung is detectable by roentgenograms, it presents no pathognomonic roentgenologic signs. The lesions seen are usually confounded with tuberculosis, bronchiectasis, pneumonia, and neoplasms. The differential diagnosis from tuberculosis and the acute infections is not so difficult. While in cases of neoplasms necropsy assists in the differentiation, the authors point out the importance of developing a biologic method that would make certain the diagnosis, such as attempts to recover *Treponema pallidum* from lung tissue.

ANTONIO MAYORAL, M.D.

## THE TESTIS

Discussion on Diagnosis and Treatment of Neoplasms of Testis. Proc. Royal Soc. Med., **32,** 663–670, April, 1939.

Dr. W. M. Levitt: The growth should be removed, if practicable, before irradiation. Of 18 cases radiated at St. Bartholomew's Hospital, from 1930 to 1935, five were alive in September, 1938, and 13 were dead. There were three five-year survivals still living. Metastases, even general, may be eliminated for long periods. Therefore, prophylactic irradiation of the most frequent sites of secondary deposit is indicated. This should include the pelvis, groins, and homolateral lumbar glands, as well as the central aortic glands.

Of nine cases prophylactically radiated between 1929 and 1934, five were alive in September, 1938, and four were dead. There were five five-year survivals; four are still living. This compares with Hinman's tabulation of 6.5 per cent of five-year survivals in 258 patients treated by orchidectomy only.

In deciding the scope of prophylactic radiation, one must balance the prospective improvement of results against the heavier demands on the patient's condition.

With metastasis, test doses should be used to determine radiosensitivity. The "x-ray-bath" method, developed at St. Bartholomew's Hospital, in radiosensitive cases permits the exposure of large regions, or even the whole trunk, to doses of x-rays which are not very much smaller than those applied to localized lesions. Radiation must be administered cautiously at first to avoid toxic effects.

Radium is not indicated in the treatment of testicular tumors. The favorable prognosis of testicular tumors is not as widely realized as it should be.

Mr. Reginald T. Payne: The usually gloomy prognosis given for testicular tumor is protested by Mr. Payne. Of 38 cases operated upon from 1920 to 1933, two died of operation, 14 of disease, four were not traced, 18 had cures of five years and over. There were 19 teratomas and 19 seminomas. Five-year cures included nine of each.

The duration of symptoms before operation for the whole group was 7.5 months. For the five-year cures, 6.9 months; for those dying from disease, 8.7 months. Radiation had been given to eight of 14 patients dying with disease and to seven of the 18 five-year survivors.

Diagnostic mistakes include removal of gummatous testicle, failure to recognize carcinoma in hematocele, or supposed idiopathic hydrocele. Quantitative use of the Aschheim-Zondek test is valuable and the response to radiation closely linked with prolan A excretion.

Local operation and radiation give the best results. The disconcerting late recurrences require an adequate follow-up with regular clinical and biologic tests.

RAY A. CARTER, M.D.

## THE THYMUS

Lymphosarcoma of the Mediastinum (Malignant Thymoma): A Clinical and Pathological Study, with Case Report of a Child. Edward J. Bomze and Jack D. Kirschbaum. Jour. Lab. and Clin. Med., **24,** 928–934, June, 1939.

In this article the authors give a review of the literature on malignant tumors of the thymus gland and of tumor-like growths of the thymic region with the clinical and pathologic study of a case report of a child. Emphasis is placed upon the importance of early diagnosis, especially since the lymphosarcomatous type is radiosensitive.

These writers believe the most important diagnostic measures to be the roentgenographic and fluoroscopic examinations of the chest.

WILLIS A. WARD, M.D.

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The Problem of the Thymus in Children. A. Graeme Mitchell and Josef Warkany. Jour. Am. Med. Assn., **112,** 283–285, Jan. 28, 1939.

The thymus cannot be entirely disregarded as a potential source of disturbance in early life, even though it has been too often incriminated by uncritical diagnosticians and too frequently treated by enthusiastic therapeutists. It is a demonstrable fact at necropsy that the thymus can cause compression of the trachea, blood vessels, and perhaps the recurrent laryngeal and other nerves and tracheal compression has been demonstrated during life by tracheoscopic examination.

Thymic stridor should be noticeable in inspiration as well as expiration. It should be continuous, diminishing only moderately during rest and sleep. Cyanosis in thymic hyperplasia may be due to imperfect aeration caused by tracheal stenosis or to compression of the large vessels which are situated near or, in the newborn period, even in the thymic tissue. Inspiratory retractions are not typical of thymic hyperplasia. Roentgenograms can be helpful in the diagnosis of thymic hyperplasia only in the hands of experts who know how to use and interpret them. Radiologic treatment is not indicated simply because the thymus

appears on the roentgenogram to be enlarged. No harm should result from one to three radiologic treatments properly given. Granted that there is such a condition as lymphatic diathesis, any enlargement of the thymus would be only an indication of the abnormal constitution, and no improvement could be expected by treatment of this organ.

CHARLES G. SUTHERLAND, M.D.

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Radiology's Responsibility in the Diagnosis and Treatment of Thymic Hyperplasia. Clyde K. Hasley. Jour. Am. Med. Assn., **112,** 285–288, Jan. 28, 1939.

From an anatomic standpoint the thymus is intimately associated with other structures of the mediastinum, such as the aortic arch and the superior vena cava. No study of the chest for thymic hyperplasia is complete without a fluoroscopic study and without roentgenograms made with the patient in three or four different positions and in different phases of respiration and of the cardiac cycle. The size of the thymus, which varies with the mediastinal shadow in the different phases of the cardiac cycle and of respiration, cannot be accepted as the actual measurement of the thymus when an incomplete roentgenographic study is made. In only a small percentage of cases is roentgen therapy actually needed. If it is deemed advisable to try a therapeutic exposure, treatments should be given cautiously in order that there may be no delayed x-ray effects. A technic which corresponds much to that used for ordinary infection has produced the desired result in the author's experience.

CHARLES G. SUTHERLAND, M.D.

## THE THYROID

Radiation Control of Hyperparathyroidism. Edwin A. Merritt. Jour. Iowa St. Med. Soc., **29,** 373–377, August, 1939.

The author discusses the clinical aspects of hyperparathyroidism and the uses and value of radiation therapy in the treatment of this disease. Schilling's clinical classification is considered simple and adequate and lists three major clinical forms: (1) typical bone lesions in which osteitis fibrosa predominates; (2) the more common form characterized by local or general demineralization of bone but without cyst formation, and (3) calcium deposits in the lungs, joints, and especially the kidneys (renal calculi). The chief complaint, usually, is pain, located at the site of the most severe demineralization. In the more extensive forms of the disease, there is anorexia, weight loss, and asthenia. Indigestion and constipation are common. The blood picture is that of a secondary anemia. Roentgenologically, the presence of multiple bone cysts distributed throughout the skeleton is characteristic but may be simulated to some extent by multiple myeloma. In the osteoporotic form, with no cysts present, the picture is one of demineralization, commonly granular. The spine may be involved alone with collapse of multiple vertebral bodies. At times hyperparathyroidism may be indistinguishable from multiple myeloma, basophilic adenoma of the pituitary, or metastatic carcinoma.

The author and his associates have found radiation therapy a highly efficacious measure in the treatment of this disease. Prompt relief from pain is to be expected. Ordinarily, 200 r is given to the parathyroid area daily for five days. Two such series at an interval of six weeks is usually sufficient. Recalcification is slow and does not follow as rapidly as the improvement in clinical symptoms.

LESTER W. PAUL, M.D.

## THE TIBIA

Pseudofracture of the Tibia. Sumner M. Roberts and Edward C. Vogt. Jour. Bone and Joint Surg., **21,** 891–901, October, 1939.

In the early roentgen examination of this condition, which occurs in the upper third of the tibia, the posterior border shows periosteal thickening as with an infection. This condition increases and later a break in the cortex can be seen which penetrates deeper into the bone and may involve almost the entire thickness of it. Biopsy shows evidence of chronic infection. With rest and plaster support, all cases have healed without undue results. Of 12 patients encountered, one had a true spontaneous fracture.

The condition occurs between the ages of four and sixteen years. Trauma is not an etiologic factor. The exact nature of the condition is unknown, but there is a similarity to "march foot."

JOHN B. MCANENY, M.D.

## TUBERCULOSIS, PULMONARY

Tomography (Body-section Roentgenography) as a Diagnostic Aid in Pulmonary Tuberculosis. Miguel Cañizares, Cirilo Santos, Andres A. Angara, and Manuel Lahoz. Bull. Quezon Inst., **1,** 5–19, July, 1939.

The authors discuss the origin of the science of tomography (planigraphy) and its development in theory and practice. The value of tomography is readily seen when we consider that a mere 40 per cent of the pulmonary parenchyma is not covered by one or more of the bones of the chest. (This method is of value in the skull, spine, shoulder joints, and mediastinum in particular.) Tomographic fluoroscopy is an aid in positioning the plane prior to plate making. A tomographic series may reveal an uncompressed cavity within an apparently collapsed lung; the direction, extent, and width of pleuritic adhesions in a pneumothorax; the presence of a cyst wall which may differentiate a cyst from a newgrowth; may outline stem and secondary bronchi; foreign bodies within the lumina of bronchi, and a wealth of material to the bronchoscopist previous to instrumentation. Tomography makes the study of the mediastinum comparatively easy; easily diagnoses the beginning of Pott's disease in the thoracic spine, and eliminates confusing lines in skull films.

The authors have written an informative article describing a new method for the study of disease when other possibilities have been exhausted, and in cases in which human life is the stake involved.

W. H. GILLENTINE, M.D.

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A Program for Early Aggressive Treatment of Pulmonary Tuberculosis. Casper F. Hegner. Jour. Am. Med. Assn., **112,** 136–141, Jan. 14, 1939.

A program for early aggressive treatment of pulmonary tuberculosis is properly initiated by the diagnosis of the disease in the earliest possible stage. During the period of inception and the early stage more can be accomplished by less therapy than at any time thereafter.

The inception of tuberculosis is subtle, the onset insidious, and the early progress stealthy and so devoid of symptoms that the host is taken unawares. The preclinical and early clinical stages are often overlooked even by expert examiners.

The tuberculin test must be used with children and in all suggestive cases fluoroscopic examination must be done and roentgenograms of the chest made. To be dependable, x-ray examinations must be interpreted by experienced physicians or experts in pathologic changes of the lungs as depicted by x-ray examination. In borderline cases the x-ray examination cannot determine the grade of activity of a tuberculous lesion. It does portray more accurately than any other diagnostic procedure the presence and extent of lesions. It is obligatory to check the physical signs with those shown by x-ray examination.

To wait for the disease to become clinically manifest is to wait too long. Prophylaxis is certain, while cure is uncertain when the disease is fully developed and impossible in a fairly fixed percentage of cases.

Delay in diagnosis has been and is the chief obstacle in the control of pulmonary tuberculosis. Delay in instituting the proper procedure for collapse therapy comprises and may defeat all efforts to cure.

CHARLES G. SUTHERLAND, M.D.

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The Detection of Tuberculous Infection: Comparative Value of the Pathologic Examination, the Tuberculin Test, and the X-ray Examination. J. Arthur Myers. Jour. Am. Med. Assn., **112,** 1904–1910, May 13, 1939.

It is almost fruitless to make x-ray films of the thorax of children, even though they react strongly to tuberculin, before they reach the age of adolescence. It is practically fruitless to make x-ray films of the thorax of children who react to tuberculin to find evidence of the lesions of the primary complex. Studies have led the author to believe that x-ray examination of the thorax of children is almost a total waste, as far as tuberculosis is concerned.

However, when the period of adolescence is reached and on through the span of life, every tuberculin reactor should have x-ray examination of the thorax annually, as long as no significant shadows appear, and much more frequently if shadows do appear which may be due to clinical tuberculosis.

Patients who present such shadows are subjected to complete examination, including laboratory studies of the sputum and the gastric contents for acid-fast bacilli, periodic red cell sedimentation tests, observation for symptoms, examination for abnormal physical signs, and frequent x-ray examinations of the thorax to determine whether or not the shadows persist, and, if so, whether they change.

The diagnosis of tuberculosis often is made only with extreme difficulty; there are no short-cuts, such as a single x-ray examination.

CHARLES G. SUTHERLAND, M.D.

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The Tuberculosis Problem Viewed in the Light of Recent Pathologic Studies. Henry C. Sweany. Minnesota Med., **22,** 595–610, September, 1939.

The author presents an exhaustive review of the subject.

In the first infection, which may be at any age, but more typically in childhood, the exudative lesion may vary from 1 to 10 cm. in diameter. This may be taken up by the blood stream, or may regress and become calcified. When the latter event takes place, the tuberculin reaction may become negative.

Disease emanating from the primary infection—"endogenous reinfection"—may include a local spread with rupture or overflow into the blood stream; lymphatic dissemination; enlarged nodes around the bronchi and hilum, leading to hilum catarrh of Ranke; atelectasis, or a lobitis tuberculosis.

Exogenous infection may be superinfection on another smouldering process or may be reinfection on a completely healed process—all types of pathology of reinfection being possible. The parenchymal disease in these types usually begins in the upper and posterior portions of the lung, commonly along the subapical bronchi, in progressive disease, less commonly in the apex, the horizontal rami, and in the apex of the lower lobes.

It is practically impossible to tell the primary lesions in adult life from the reinfection type, except by the aid of the tuberculin test.

All of the phases outlined at the beginning of the article are elaborated upon and illustrated with many case reports.

PERCY J. DELANO, M.D.

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End-result of a Tuberculosis Case-finding Project. J. B. Novak and J. S. Kruglick. Jour. Am. Med. Assn., **112,** 1452–1454, April 15, 1939.

Prior to the advent of the x-ray and tuberculin test, physicians depended on contact history, subjective symptoms, and physical examination for the diagnosis of tuberculosis. The objection to these methods was that the cases uncovered were almost invariably in an advanced stage and treatment was either prolonged or unsuccessful. With the perfection of the x-ray suspected cases could be checked. This led to earlier

diagnosis but it was still not conducive to group work. With the tuberculin test and increased knowledge of tuberculosis, physicians turned to group testing. The true purpose of this work is to discover disease in the incipient stage, when treatment is more successful. In any case-finding project, one can determine (using two or three tests) almost 100 per cent of those infected with tuberculosis. Large-scale testing can be done at a relatively low cost. The positive reactors can be roentgenographed and tuberculous disease determined long before the patient shows subjective signs.

A study of some 65 cases of tuberculosis among the high school students of Chicago and its suburbs demonstrated to these observers the inadequacy of treatment and of follow-up. Failure to teach and impress the patient resulted in negligence on his part. The tendency to minimize the observations resulted from the failure of the physician to reconcile tuberculosis to a minimal, seemingly harmless lesion on the roentgenogram in a robust physical specimen. Patients with a positive tuberculin reaction and negative roentgenographic findings should have subsequent routine examinations to insure complete success of the campaign against tuberculosis.

CHARLES G. SUTHERLAND, M.D.

## TUMORS (DIAGNOSIS)

Calcifications and Decalcifications in Tumors of the Region of the Sella: Anatomic-radiologic Findings. P. Wertheimer, J. Dechaume, and Alfred Lévy. Bull. et mém. Soc. de radiol. méd. de France, **27,** 28–31, January, 1939.

The anatomic and radiologic findings in three cases of tumor in the region of the hypophysis are given in some detail. It is important to differentiate the destruction caused by actual invasion of the bone from that caused by pressure, as this information is of great diagnostic value.

S. R. BEATTY, M.D.

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Multiple Intracranial Tumors: A Discussion of the Relation of Meningeal to Acoustic Tumors and a Report of a Case. W. J. Gardner and O. A. Turner. Jour. Am. Med. Assn., **113,** 111–113, July 8, 1939.

Generalized von Recklinghausen's disease has been long recognized as a familial disorder. Only recently, however, has it been shown that central neurofibromatosis is also hereditary in that special form of the disease and may be transmitted as a dominant trait with little or none of the peripheral manifestations of the disorder.

A special variety of central neurofibromatosis, bilateral acoustic tumors, has been described and also established on a familial and hereditary basis. The tendency for the acoustic nerves to be involved in central neurofibromatosis was noted; in most reported instances unilateral or bilateral acoustic tumors were present as part of the diffuse involvement of the cranial nerve sheaths by their specific tumors. There was usually some associated involvement of the meninges by their specific growths, but the degree varied considerably in the reported cases. The fact that gliomas as well as meningeal tumors were present in this condition led to the concept that central neurofibromatosis was actually a disease process which involved all the binding tissues of the nervous system, including in its final picture specific tumors of the nerve sheaths, enveloping membranes and interstitial tissues of the central nervous system.

Unilateral (or solitary) acoustic tumors are relatively common and as far as can be determined at the present time bear no relationship to von Recklinghausen's disease or central neurofibromatosis. The authors report a case of the association of a unilateral acoustic tumor with a meningeal growth in which von Recklinghausen's disease played no apparent part.

CHARLES G. SUTHERLAND, M.D.

## TUMORS (THERAPY)

New Results in the Near Distance Radiation of Malignant Melanoma. K. Greineder and W. Neumann. Strahlentherapie, **66,** 89–95, 1939.

The authors report their experience with the treatment of 25 cases of malignant melanoma by means of near distance radiation. In 88 per cent, the primary tumor disappeared and at the time of writing 52 per cent of the patients were still free from symptoms. Five of the patients were under observation less than a year, four from one to two years, six from two to three years, four from three to four years, four from four to five years, and two for five years. The technic is as follows: 60 kv., 0.2 mm. Cu, 5 cm. F.S.D., daily dose of 400 to 500 r with total doses of 10,000 r. They also treated nine patients who had a recurrence after surgical removal of the tumor. Five of these died within from 9 to 18 months after the treatment and four were still alive after two- and three-year observation periods. In view of the well known radioresistance of the melanoma, the results obtained with the authors' method must be considered encouraging.

ERNST A. POHLE, M.D., Ph.D.

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Is the Near Distance Irradiation According to Chaoul Suitable for the Treatment of Deeply Infiltrating Tumors? Z. Hrabovszky. Strahlentherapie, **66,** 119–131, 1939.

The author has seen good results in the treatment of carcinoma of the skin by near distance radiation. He also tried the method in some cases of carcinoma of the rectum, urethra, vulva, and penis. Although the number of cases treated in the latter group is small (total to date, 15) he obtained very encouraging response in some. As in carcinoma of the rectum, it is necessary to combine the treatment with surgery (exposure of tumor). Metastatic nodes are removed if they have not grown through the capsule; the inoperable ones are treated by interstitial radium, teleradium, or roentgen therapy. For superficial nodes, near distance radiation is the method of choice.

ERNST A. POHLE, M.D., Ph.D.

Roentgen-ray Studies of Mediastinal Tumors. Charles H. Peterson. Southern Med Jour., **32,** 517–522, May, 1939.

Seven cases of mediastinal tumors, clinically diagnosed as malignant, are reported with roentgenographs of the chest illustrating the tumors. X-ray therapy was given in relatively small doses, with the result that two patients were well after seven years and one after five years.

It was noted that clinical improvement occurred within one or two hours after the initial treatment. A similar reaction time was noted in the treatment of persistent thymus causing obstruction. In a case of leukemia the blood count was found to be lowest one and one-half hours after treatment. A test dose of roentgen-ray therapy is suggested for all non-pulsating tumors of the mediastinum.

JOHN M. MILES, M D.

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Recommendations for the Use of Near Distance Radiation in Epithelioma of the Skin. H. G. Bode and H. Kliegel. Strahlentherapie, **66,** 96–107, 1939.

The authors briefly discuss the experience at the Dermatological Clinic of the University of Breslau, with the use of near distance radiation in epithelioma of the skin. For basal-cell carcinoma they recommend a single massive dose of 2,000 r, while all others should be treated with the fractional method, giving total doses of from 4,000 to 10,000 r. Of basal-cell carcinoma treated until August, 1938, 98.6 per cent of 296 patients remained well. The corresponding figure for 112 cases of squamous-cell carcinoma was 92 per cent. All these patients had been studied for a period of from one to four years. A series of photographs are shown in the article demonstrating some of the remarkable results which can be obtained even in far advanced lesions.

ERNST A. POHLE, M.D., Ph.D.

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The Radiosensitivity of Malignant Melanomas. Frank Ellis. British Jour. Radiol., **12,** 327–352, June, 1939.

The melanomas are generally regarded as being insensitive to radiation in spite of the fact that there is considerable evidence to show that they are sensitive. Inadequate treatment in the past may account for this opinion.

Thirty-eight cases of malignant melanoma are reported. In 12, radiotherapy can be accounted successful, in two the result was doubtful, in seven cases radiation failed, in 13 the result was indefinite, and four were not treated.

In all the cases that failed there was a history of trauma or operation. Inefficient treatment was also contributory to the failure in some instances.

The average age of the patients at the time of treatment was 47 years. Successful treatment occurred in areas where there was good blood supply. If the dose of radiation was either too low or too high, the result was failure.

In spite of the fact that metastasis occurred early and was rather promptly fatal, the response of the primary lesion to radiation indicates that malignant melanomas are sensitive.

SYDNEY J. HAWLEY, M.D.

## THE URINARY TRACT

Suppression of Urine Complicating Pyelography. William C. Quinby and George Austen, Jr. New England Jour. Med., **221,** 814–816, Nov. 23, 1939.

This article reviews the various agents used in intravenous pyelography and describes their composition. It is noted that these iodine-containing compounds are excreted from the kidneys by the tubules and it is suggested that this could be used to differentiate between the function of the tubules and the glomeruli. It is also known that absorption from the renal pelvis can occur, as shown by study of the blood after the injection of sulphanilamide into the pelvis of the kidney.

Four case histories are presented in which retrograde pyelography followed intravenous urography immediately or within 48 hours, with resultant anuria. It is believed from these experiences that when renal function is reduced it is unwise to use these two procedures within so short a period of time.

JOHN B. MCANENY, M.D.

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Hydronephrosis Secondary to Non-calculous Ureteropelvic Obstruction. Walter I. Buchert. Pennsylvania Med. Jour., **43,** 625–630, February, 1940.

The usual causes of non-calculous obstruction of the ureters may be placed in four groups: (1) anomalous renal vessels; (2) stricture of the ureteropelvic junction; (3) peripelvic connective tissue or fibrous bands; (4) obstruction due to lateral insertion of the ureter. A combination of intravenous urography and retrograde pyelography is recommended, as is a film in both the recumbent and upright positions. The general types of surgery which may be performed are briefly discussed.

JOSEPH T. DANZER, M.D.

## THE UTERUS

The Treatment of Carcinoma of the Cervix Uteri: Tissue Changes During and Following Radiation Therapy. J. Cash King and W. W. Brandes Southern Med. Jour., **34,** 233–239, March, 1939

Important phases in the treatment of cancer of the cervix include prophylactic repair and treatment of cervical lesions, elimination of infection, Wassermann test, constitutional measures to prepare the patient for radiation, and a co-operative frame of mind in the patient and her family. Roentgen-ray therapy is applied before radium. Using 70 cm. distance and six portals over the pelvis, the greatest amount of radiation is delivered to the parametrium. From 1,500 to 2,000 r are given to each field over a period of three weeks. This gives three threshold erythemas in the parametrium.

Greater irradiation in the parametrium is desired, five or more erythemas being recommended. Additional irradiation can be obtained by (*a*) supervoltage roentgen therapy; (*b*) intravaginal roentgen therapy, and (*c*) interstitial radium in the paracervical tissues.

The changes produced by radiation therapy are studied by serial biopsies obtained during treatment. Such biopsies are not to be relied upon as the sole index of cure.

JOHN M. MILES, M.D

## THE WRIST

Wrist and Ankle Injuries. F. J. Morrin. Irish Jour. Med. Sci., **165,** 656–659, September, 1939.

In injuries about the wrist, Morrin stresses the fact that fracture of the scaphoid is frequently misdiagnosed as a sprain, and dislocation of the semilunar is usually not recognized. Proper reduction of a Colles' fracture should show the articular surface of the radius in the anteroposterior view to be at an angle of 30 degrees with the true horizontal, while the lateral view should show the articular surface to be at right-angles to the axis of the bone.

Injuries about the ankle joint may show no fracture, but spreading of the mortice may be present, and, if untreated, great disability may result, with deformity of the involved bones. With actual fractures, subluxation of the ankle may be present and must be recognized. Fractures of the anterior or posterior lips of the tibia may occur and are usually readily reduced but difficult to maintain.

JOHN B. MCANENY, M.D.

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Kienböch's Disease of the Lunate. Edwin F. Cave. Jour. Bone and Joint Surg., **21,** 858–866, October, 1939.

Cave describes the aseptic necrosis of the carpal lunate, familiarly known as Kienböch's disease, and gives a short historic review of the condition. He is of the opinion that trauma, direct or indirect, is always the cause. Of five cases, one followed dislocation of the lunate.

Microscopic examination of a diseased lunate removed at operation showed extensive necrosis consisting of amorphous eosinophilic substance with little exudative reaction. The surface showed discrete areas of chondrolysis. Except for the necrotic areas, the marrow showed dense fibrosis associated with lymphatic and phagocytic infiltration. Foreign-body giant cells are occasionally observed.

In the roentgenogram, the earliest changes are seen in the proximal portion. There are some areas of increased density and others of decreased density. With time, the density increases, the bone becomes smaller and irregular. Fragmentation may occur.

The diagnosis depends upon the roentgenogram.

JOHN B. MCANENY, M.D.